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ISBI Practice Guidelines for Burn Care, Part 2☆

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Introduction

1. Background

Burn care is a multifaceted process that spans multiple settings, ranging from initial injury and on-site care to long-term follow-up and reconstruction. This edition of practice guidelines (PGs) for burn care are an extension of the PG-development project of two years ago, which was inspired by Dr. Ahuja and adroitly spearheaded by Dr. Peck [1]. Part 2 of the guidelines extends the recommendations addressed in the first guidelines by addressing different aspects of ongoing burn care and addressing special types of injuries frequently treated in a burn unit. As with the first set of guidelines, the PGs in this document are recommendations for diagnosis and treatment of burn injuries. The recommendations were developed through an assiduous interactive process among a dedicated panel of experts who utilized systematic reviews of the literature as well as assessments of the benefits and harms of the presented options to define the most effective and efficient methods of evaluation and management [2–6].

The mission of the ISBI Practice Guidelines Committee is to create clinical guidelines to improve the care of burn patients and reduce costs by outlining recommendations for management of specific medical problems encountered in burn care. Recommendations are supported by objective and comprehensive reviews of the literature as well as by expert opinion. Our vision is that these guidelines for burn care will recognize the current best and most cost-effective methods of burn treatment to guide resource-limited settings (RLS) and burn care throughout the world.

The objectives for PGs continue to include standardization of care, quality improvement, reduction of risk, and optimization of cost-benefit ratios. As such, the PG recommendations focus on important clinical options, critical decision points, and subsequent clinical response which will influence outcomes. The degree to which these recommendations are crafted upon evidence-based medicine hinges on the existence of high-class scientific studies, the concurrence of conclusions among published studies, and the consensus of experienced practitioners, which can be problematic in burn care, particularly in RLS. Ultimately, the utility of PG recommendations may rest less on scientific certainty and more on the establishment of goals for care based on costs, benefits, potential harms, values and preferences.

Part 2 of the guidelines maintains the standards set in Part 1, including validity, reliability and reproducibility, clinical applicability, clinical flexibility, clarity, multidisciplinary process, scheduled review, and documentation [2]. PG construction was a standardized yet punctilious process, again following the Guidelines Review Committee of the World Health Organization (WHO) in the *WHO Handbook for Guideline Development* [7].

The International Society for Burn Injuries (ISBI), recognizing the need to provide burn care practitioners with recommendations for patient care, adopted the motto “One World, One Standard of Care” in 2012 to directly address the need for harmonization of burn care practice across the world. Worldwide, the best clinical outcomes after burn injury hinge on this process.

Part 1 of the guidelines undertook the challenge of guiding a panel of burn experts through the process of writing much needed PGs, applicable in all settings regardless of resource availability. Mission and vision statements, composition and function of the subcommittees, elaboration of the list of topics

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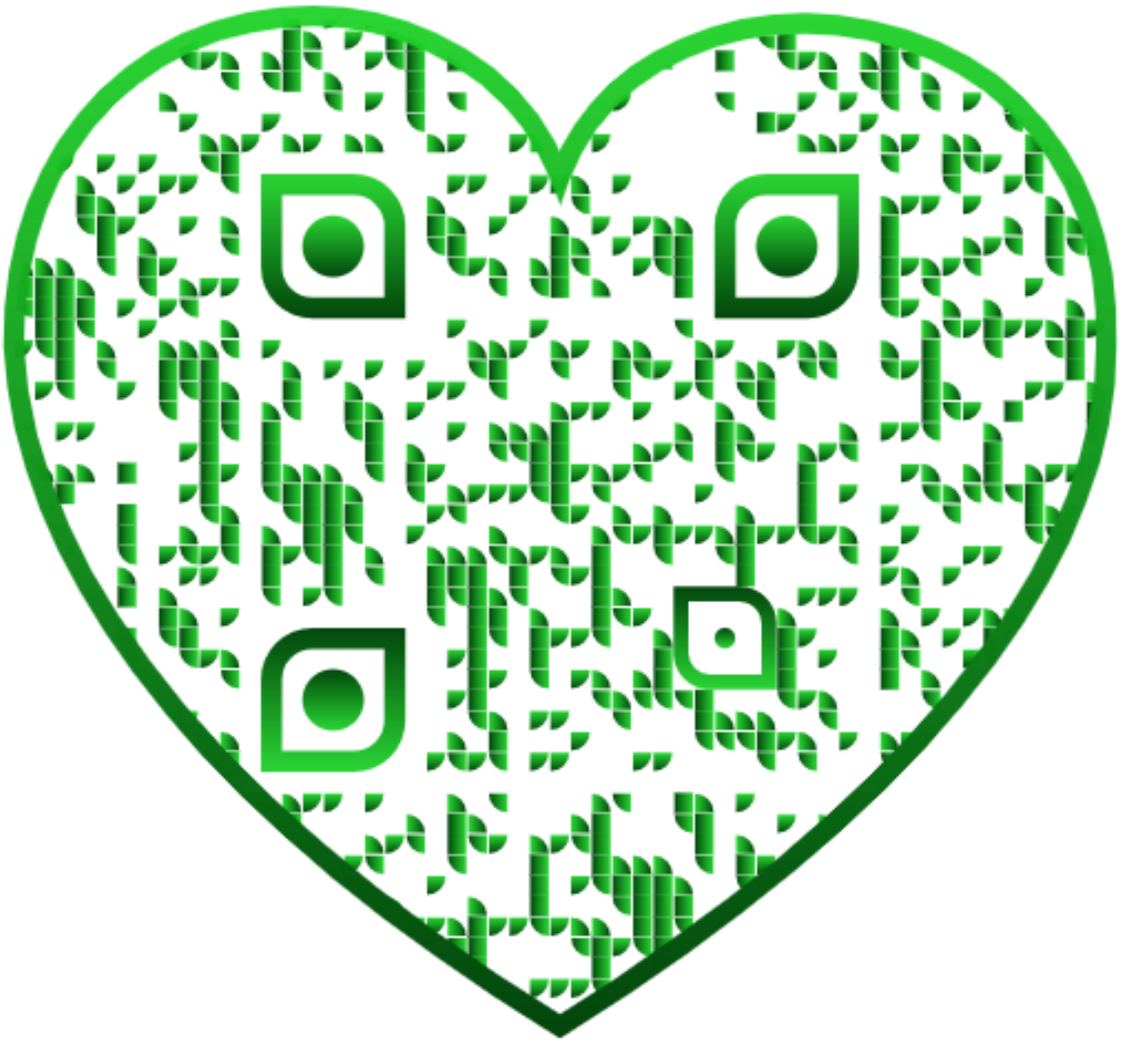

to be addressed, description of the terms of reference, visualization of the end product, and creation of a broad time frame for completion soon followed. The development and completion of the first international burn PGs followed. Part 2 of the guidelines was an extension of that process.

These PGs, intended for a primary audience of health professionals responsible for providing acute care and rehabilitation for burn patients, focus on the multifaceted aspects of acute burn care. The PGs have been crafted to include recommendations germane to burn care, including in RLS. Development and application of global evidence-based recommendations that will improve patient care that accommodate all resource settings is not practical. Not every guideline can be followed by every person in every center. Local resources may indeed restrict what can be done. However, PGs can be the nidus for process improvement in all settings, including RLS. As such, guidelines are a guide, not a mandate, and should serve to help centers improve their care of the burn patient. These PGs can also be used by policy-makers, public health experts, and hospital managers to prioritize resources. The information in these PGs can be included in pre- and in-service training of health professionals to improve their knowledge, skills, and performance in burn care.

2. Methods

As was done with the Part 1 guidelines, the ISBI Practice Guidelines Committee was divided into two subcommittees: the Steering and the Advisory Subcommittees. The Steering Subcommittee performed editorial functions, conducted literature reviews, researched additional expert opinion sources, ensured uniform quality throughout the document, and confirmed adherence to structure format. The Advisory Subcommittee, who were experienced in providing burn care in RLS or were Regional Representatives on the ISBI Executive Committee, focused its content review on the proposed protocols for value (effectiveness/cost), feasibility, and preferences. The bulk of the work was accomplished by email communications using a modified Delphi method. All 32 committee members completed conflict-of-interest forms; none of these declared a potential conflict of interest in the subject matter.

Table 1 – Topics developed in current ISBI practice guidelines.

First aid
Topical agents in burn care
Infections in burns
a. Sepsis
b. Pneumonia
c. Urinary tract infection
d. Wound infection
Management of indwelling catheters
Blood transfusion
Metabolic manipulation
Mobility, strength, and physical function
Deep venous thrombosis
Pain control
Sedation
Psychiatric disorders
Outpatient burn care
Electrical burns
Chemical burns
Skin soughing disorders

Table 2 – Subcommittee membership.

The steering and advisory subcommittees included the following individuals

Advisory Subcommittee
Nikki Allorto (Africa)
Bechara Atieh (Lebanon)
Alberto Bolgiani (Argentina)
Pallab Chatterjee (India)
William Cioffi (US)
Peter Dziewulski (UK)
Alette de Jong (Netherlands)
Nicole Gibran (US)
Linda Guerrero (Columbia)
Marella Hanumadass (US)
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Yvonne Singer (AU)
Paul van Zuijlen (Netherlands)
Joan Weber (US)
Shelly Wiechman (US)

The Steering Subcommittee enumerated the topics to be included in Part 2 due to their clinical relevance. The finalized list of topics appears as the subjects of the individual sections in the documents that follow (Table 1). Infection, which is a major challenge in burn patients, was divided into the four most commonly encountered categories: sepsis, pneumonia, urinary tract infection, and wound infection. The development of additional important topics will occur between 2018 and 2019.

As in Part 1 of the guidelines, each member of the Steering Subcommittee was charged with developing an assigned topic,

which included review of the literature and crafting the recommendations. These recommendations were reviewed by the Advisory Committee, and adjustments to the guidelines were completed by the Steering Committee. The Steering Committee then completed the justification for each recommendation, and elucidating the balance of benefits and harms, values and preferences, and costs. After the recommendations were written, they were circulated by email among the Advisory Subcommittee for feedback. After further revisions, the recommendations and accompanying text were sent to the Advisory Subcommittee. Following the final review of all content for each topic by the Advisory Subcommittee, the chapters (topics) were then sent to the medical editor to prepare for submission to the journal editor. The process for evidence retrieval remains the same as for Part 1 of the guidelines [1].

One of the features distinguishing both Part 1 and Part 2 PGs from the work on previously published burn care PGs is the inclusion of a summary of the balance of benefits and harms of each recommendation, followed by an allusion to values and preferences, and costs, which helps address the needs of RLS. The definitions of value, preference, and cost remain unchanged from Part 1 [1].

The objective of all the ISBI guidelines remains to offer concise, evidence-based recommendations for burn care. For many of the recommendations, a paucity of evidence necessitates some imprecision in our statements. To add granularity to these recommendations, therefore, some recommendations are followed by a set of frequently asked questions (FAQs).

3. Dissemination plan

As in Part 1 of these guidelines, the ISBI Practice Guidelines are perceived as a living document with planned reconsideration on emergence of fresh, strong evidence, and there is, therefore, a commitment to undertake periodic review. The information will first be distributed through the journal *Burns*, followed by provision of open access via the Internet.

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First aid

Recommendation 1

First aid begins with the first responder at the accident site and ends when primary care commences at a health care facility. Knowledge regarding adequate first aid is globally deficient; public education is necessary to improve knowledge about first aid and to optimize first responder action.

1. Considerations in formulating Recommendation 1

First aid is the provision of immediate care to a victim with an injury or illness, usually provided by a lay person and performed within a limited skill range. After burn injuries, the bystanders are most often the initial care providers. First aid is normally performed until the injury or illness is satisfactorily dealt with or until the next level of care is started [8]. First aid must be effective and achievable by the general public, and must not hinder professional examination or later treatment. First aid interventions seek to "preserve life and alleviate suffering, prevent further illness or injury, and promote recovery" [9].

The International Federation of Red Cross and Red Crescent Societies (IFRC) states that while first aid is by no means a substitute for emergency health services, it is a pivotal primary step for providing effective and rapid interventions to reduce serious injuries and increase the chances of survival [10]. To be most effective, first aid should be provided immediately after the event. Studies conducted in developed countries on nonfatal injuries have reported that first aid plays a significant role in reducing mortality rates [11]. In developing countries, several studies have shown that first aid given by an untrained provider (e.g., caregiver, bystander) or a trained provider is generally poor but increasingly essential to reduce mortality as well as severity of injuries [11–14].

A survey by Rea et al. [15] on the practice of first aid in burns in Western Australia showed that only 39% of adults who sustained burns received appropriate first aid treatment. Cuttle et al. [16] in a retrospective study of 459 pediatric patients treated in Brisbane, Australia, with acute burns, showed that only 12.1% received what was regarded as optimal first aid. Studies from low- and middle-income countries (LMIC) showed that most of the burn cases patients did not receive any form of first aid [17–21]. It appears that the issue of inadequate first aid in burns is global with regional variations depending on the socioeconomic settings in the various regions.

Obviously, a need exists for public education about optimal first aid for burns. National statistics recognize that burns are most common in children under the age of 3 [22]. An argument has therefore been made that burns first-aid education should be provided to all parents and caregivers of infants and toddlers.

Teaching first aid in the home setting and in schools can potentially reach the vast majority of the population, and evidence suggests that first aid can be taught from a young age [23]. In order to achieve a greater first aid response to everyday injuries and illnesses, a wider dissemination of first aid skills to the public is necessary. In resource-limited settings (RLS) particularly, first aid training workshops should be regularly organized for all forms of trauma, including burns, for the community, the workplace, and health professionals. Future research should address the optimal design and implementation of such training.

1.1. *Balance of benefits and harms*

First aid provided by non-health care professionals has the potential to reduce morbidity and mortality from common injuries and illnesses, which represent a significant public health burden [24]. In order to achieve a greater first aid response to everyday injuries and illnesses a wider dissemination of first aid skills to the public is necessary [25]. Basic first aid training courses must prepare individuals from a variety of backgrounds to provide appropriate and effective treatment for a wide range of conditions [26]. However, first aid education is under-researched and insufficiently documented, meaning current practice is not evidence-based. Despite the fact that a large body of evidence exists for the correct first aid approach to the treatment of burn and scald injuries, research from a number of countries demonstrates that the public is unclear on how to provide initial treatment [27–30].

Inappropriate first aid could potentially harm the victim. In one study, individuals from ethnic minorities were more likely to perform inappropriate first aid for burns, such as applying tooth paste or butter [27]. This evidence suggests that public education on first aid for burns is necessary in many countries and should be accessible by ethnic minorities [27]. Studies that targeted those from non-English speaking backgrounds in New Zealand found that while their media intervention initially produced a drop in the need for grafting following a burn, after 5 years this effect had decreased [31]. Therefore, large educational campaigns for burns first aid could prove successful in other parts of the world, particularly in RLS, but may need to be repeated on a regular basis for this knowledge to be retained [31,32].

1.2. *Values and preferences*

It has been shown that good first aid improves the outcome of the burn patient [15] and this finding demonstrates that participation in a first aid course improves knowledge. One may argue that it is justifiable to progress toward compulsory first aid courses, including first aid for the burn patient, to improve outcomes for the community as a whole. The next step is then to re-audit the effectiveness of these campaigns, both in terms of knowledge in the community but also to re-assess the first aid our patients are receiving prior to review in the hospital [15].

1.3. *Costs*

The mandate of health systems to provide essential services has also been stressed through the rights-based approach to health. The availability of adequate emergency medical services is often considered a basic human right in high-income countries and this right should not be neglected in LMIC, which bear the disproportionate burden of injury [33]. Despite this burden in LMIC, many of these places have no formal prehospital emergency system. A simple "scoop-and-run" approach with basic life-saving interventions will be most practical and effective in the absence of second-tier responders such as paramedics who are trained in advance airway management, vascular access and fluid resuscitation [33].

Recommendation 2

The first step in first aid is to remove the subject from all potential burning sources including heat/flame, live electrical sources, and chemicals. The first responder should attend to the personal safety of themselves and bystanders.

2. Considerations in formulating Recommendation 2

First responders must know how to protect themselves from flames, fumes, toxic gases, falling masonry, and other hazards to personal safety [34]. Such rescue workers in flame burn situations must: not walk over ground covered with easily flammable material; keep away from anything containing flammable liquid that might explode; not cross floors or lofts, or use stairs, or walk under ceilings exposed to the flames; not stand downwind from the flames; and if possible, use protective clothing and devices [34]. The initial aim of first aid in flame and scald burns is to move the victim from the source of injury to a safe place. This should always take precedence over putting out the fire.

For flame burns, the "Stop, Drop and Roll" policy should be adopted. Prevent the victim from running, which would only fan the flames and make them burn faster. As flames always burn upwards, lying flat not only prevents the flames from involving the face, head and scalp hairs, but also prevents the fire from going around the body. Flames can also be put out by dousing with water; if water is not available, any nonflammable liquid such as milk or canned juice can be used [35,36]. (See sections on Electrical Burns, p. xx and Chemical Burns, p. xx, regarding the removal of the burning source.)

2.1. *Balance of benefits and harms*

The evidence for stopping the burning process derives largely from expert opinion. With regard to first aid, stopping the burn process, removing clothing and jewelry, and covering the wound with a sterile dressing would all positively affect the outcome of burns [37–40]. Once the fire has been extinguished, all the burned clothes (including belts, socks and shoes) should be carefully removed from the victim's body. Especially with scald injury in young children, it is important to remove the diaper as it can contain the agent and might continue the burning process. Fabric that has melted and is stuck to the burn wound should be left in place. Ornaments should also be removed as they retain heat and continue tissue damage for a prolonged period [35]. Rings around the fingers and toes can cause a constrictive tourniquet-like effect, severely

compromising the circulation to the distal portion of the digits once the edema sets in [35].
Topical application of ointments, creams and lotions over the burn wound should be avoided. These applications make assessment of the depth and extent of the burn wound difficult and removal of these substances may be difficult and painful to the patient. Blisters should be left intact if the victim is 24–48 h from medical attention [41–43].

2.2. Values and preferences

Putting out a fire rapidly, completely and safely is not always easy, especially when the burning person is running around frantically. This is more evident in many RLS where first aid education is poor or nonexistent. Large families live in a small space; even though the 'stop, drop and roll' policy is advocated in the case of a domestic fire, this may not be possible if space is not available. Blankets may not be available to smother the flames. Water puts out fires and also rapidly cools [44]. If a person's clothes are on fire, let the person lie down or sit down. Water should be poured over or thrown at the burning person. Wet unburned clothing does not catch fire; hence water should be used liberally.

2.3. Costs

Costs associated with this recommendation are not significant.

Recommendation 3
For heat/flame injuries, the burn wound should be cooled optimally with clean running water and with temperature adjusted to the subject's preference for 15–20 min. After cooling, the patient should be kept warm while primary medical attention is sought.

3. Considerations in formulating Recommendation 3

For centuries, cooling the burn wound has been used empirically in an attempt to reduce pain and decrease mortality. Many different recommendations regarding the first aid treatment of burn injuries have been proposed by various regulatory bodies [45–49]. These recommendations all advocate the application of using cool or cold tap water [45–49]. Although cooling is generally accepted as an adequate first aid measure, the optimal procedure remains unclear. Several factors involved in cooling may influence the effect of cooling on the burn injury, including the duration of cooling, the temperature of the coolant, the kind of coolant (hydrogels or water), and the time frame in which cooling should be started. These factors should be taken into account in any recommendation about cooling and are therefore discussed in the next paragraphs. The underlying evidence is based on animal studies, simulation models and retrospective cohort studies.

3.1. Duration of cooling

Recommendations on duration of cooling vary and are based on retrospective and prospective cohort studies, animal studies, simulation models and expert opinion. One retrospective cohort study included the charts of 458 children who presented at an Australian burn center and found no overall correlative relationship between first aid duration (either cool water $\geq$20 or $<$20 min) and re-epithelialization. Only in a subgroup of children with contact injury was first aid with cool water $\geq$20 min found to be associated with a decreased re-epithelialization time [16].
A more recent prospective cohort study examined data collected from 2897 admitted patients in Australia and New Zealand [50]. The duration of cooling was categorized as none, 1–9 min, 10–19 min, 20–39 min and 40 or more minutes. Results indicated significant beneficial effects of water first aid on several outcomes, including intensive care unit (ICU) admission, graft surgery, in-hospital death, and hospital length of stay, but did not favor one category specifically [50]. In general, the categories 1–9 min and 10–19 min were most beneficial compared to providing no water first aid. Additional analyses for influence of covariates showed that all outcomes were influenced by percentage total burn surface area (TBSA) burned and patient age. The authors concluded that first aid with water-cooling significantly reduces the need for surgical intervention, length of stay and ICU admission, particularly if applied for up to 20 min [50].
Similar results were found in several studies with porcine models that investigated the effects of temperature of the coolant (water) and the duration of cooling. Although the results of most studies indicated some beneficial effect of 20-min cooling compared to no cooling, these results should be interpreted with caution due to several limitations (small sample size, indirectness, attrition bias, reporting bias). Bartlett et al. [51] reported statistically significant improvement in burn depth on post-burn day 9 in the wounds cooled for 20 min compared to the other durations (no cooling, 5, 10 or 30 min) in 17 pigs (85 wounds). This outcome was measured with histologic assessment resulting in a mean burn depth assessment indicating superficial dermal damage in all intervention groups. Cuttle et al. [52] reported an improved re-epithelialization on week 2 with 20 min of cooling compared to no cooling, but no difference at week 3. No significant differences were found for cosmetic appearance 6 weeks post burn between the different durations of cooling (no cooling, 10, 20, 30 or 60 min) in 40 pigs (80 wounds) [52]. In another study by Cuttle et al. [38], the effects of different cooling temperatures were investigated in 29 pigs (58 wounds). Results showed faster full re-epithelialization with 20 min of cooling (4.0 weeks) compared to no cooling (4.5 weeks) [38]. Other animal studies reported beneficial effects of cooling compared to not cooling without presenting a statistically significant result [53,54].
Two studies [55,56] used simulation models to determine the effect of cooling. Both concluded that a beneficial effect of cooling could not be explained solely by the reduction of temperature of the wound [55] but that other biochemical processes must be influential [56]. The simulation model of Baldwin et al. [56] also indicated the cooling for more than 30 s had no additional effect from a heat-transfer point of view.
The evidence on optimal duration of cooling is insufficient in order to draw any definite conclusions. Nonetheless, experts around the world acknowledge cooling as an adequate first aid measure and generally recommend cooling up to 20 min. Prolonged cooling ($>$20 min) increases the risk of hypothermia

and subsequent negative effects on the burn injury. Based on the evidence and expert opinion, a cooling duration of between 15 to 20 min seems adequate.

3.2. *Temperature of coolant*

Recommendations on the temperature of the coolant are based on retrospective cohort studies, animal studies, simulation models and expert opinion.

Two retrospective cohort studies investigated the role of cooling on hypothermia. Singer et al. [57] reported 15 cases of hypothermia in 929 emergency department presentations of patients with burn injury, but none of these patients received prehospital cooling. Hypothermia was found to be related to the severity of the burn injury. Lönnecker and Schoder [58] reported similar findings in 212 adults admitted to a burn unit: no influence of cooling only on the body temperature, and hypothermia only occurred in the anesthetized and artificially ventilated patients. In a study by Cuttle et al. [38], the effect of different temperatures of cooling was investigated in 29 pigs (58 wounds). Results showed faster full re-epithelialization with 20 min of cooling with water of 2°C or 15°C (4.0 weeks) compared to no cooling (4.5 weeks) or cooling with ice (4.7 weeks). Similar results were found in Venter et al. [54] in 10 pigs (40 wounds); cooling with ice water (1–8°C) resulted in more tissue damage compared to no cooling and cooling with tap water (12–18°C) resulted in less tissue damage compared to no cooling [59]. A simulation model indicated only a minimal difference between the efficacy of 10 s cooling with cold water (1°C) and lukewarm water (25°C). The efficacy remained similar, even up to cooling with water at 55°C [56].

The evidence on optimal temperature of coolant is insufficient in order to draw any definite conclusions. Nonetheless, experts around the world acknowledge that cooling with ice water or cold water might increase the risk of hypothermia and subsequent negative effects on the burn injury. Furthermore, application of cold water may be unpleasant for the patient which might result in early termination of cooling. Based on the evidence and expert opinion, a temperature adjusted to the patient's preference seems adequate and most favorable for compliance of cooling.

3.3. *Kind of coolant*

Recommendations on the kind of coolant to use are based on expert opinion. The way in which water treatment is applied to the wound appears to be important. Methods of application of water in the cooling process include cool soaks [35,53,60], cool running water [45–53], water spray [53], or immersion in cold water [64,65]. To date there have been no studies that test immersion of the burn in cool water compared to treatment with swabs soaked in water, sprays or running water.

No identified studies investigated the efficacy of cooling with hydrogels compared to running water. An animal study comparing running water with wet towels, water spray, or no cooling in 10 pigs (40 wounds) reported beneficial effects of cooling with running water but without showing a statistically significant result [53]. Another animal study compared providing no cooling with cooling with aloe vera, saliva, and a tea tree oil-impregnated hydrogel dressing in 8 pigs (16 wounds). Results showed no statistically significant differences between groups with regard to re-epithelialization or cosmetic appearance 6 weeks post burn [59].

The evidence on optimal kind of coolant is insufficient for drawing any definite conclusions. As running water is inexpensive, readily available in first aid situations and easy to apply, this would be the treatment of choice. In the absence of running water, hydrogels can be used as an alternative.

3.4. *Time in which cooling should be started*

Recommendations on the time within which cooling should be started are based on animal studies, simulation models and expert opinion.

In Rajan et al. [61], 12 pigs (48 wounds) were cooled with running water at 22.4°C for 20 min. Cooling started immediately after the creation of the burn injury, with a delay of 5, 20 and 60 min. No statistically significant differences were reported regarding the depth of the burn and wound healing 9 days post burn. Cuttle et al. [52] reported an improved re-epithelialization on week 3 with 20 min of cooling and a delay of 180 min compared to not cooling. There were no data on the re-epithelialization with immediate cooling or with a delay of 10 or 60 min, but figures showed similar re-epithelialization compared to no cooling in 40 pigs (80 wounds). Venter et al. concluded that cooling with a delay of 30 min resulted in less tissue damage compared to no cooling in 10 pigs (40 wounds), but this was not based on statistically significant results [54].

The evidence on the time within which cooling should be started after the injury is insufficient for drawing any definite conclusions. Nonetheless, experts around the world acknowledge the analgesic effect of cooling with water, even with a delay in onset of cooling. Therefore, delayed cooling could be applied for patient comfort while other analgesics such as paracetamol can be administered [62].

Updated recommendations for cooling in first aid [62] document that first aid should consist of cold running water, applied as soon as possible after the burn injury has occurred, and for 20 min duration (10 min to 1 h is acceptable) as this treatment has been shown to significantly reduce tissue damage, improve wound re-epithelialization, and reduce scarring. As cold water at 2°C and 15°C were both beneficial, cold water from the tap should be effective, even in colder parts of the world [62]. Ice does not appear to be as effective as running water on the healing burn wound [54,62,63]. As first aid treatment is often applied only to relieve pain, the preferred duration of the treatment may be to continue until the patient feels no pain on removal of the cold [63–66]. However, various researchers have recommended durations of 30 min to 3 h [67–69].

3.5. *Balance of benefits and harms*

The use of cold water treatment as first aid for burns has the greatest volume of supporting literature compared to other therapies, and it has been a popular treatment throughout history [37]. Cold water is believed to initially act on burn wounds to stop the burning process by cooling the tissue below the temperature required to cause injury [70]. Cold water is also believed to stabilize the vascularization and diminish the inflammatory response caused by the injury [37], and assist

burn wound healing by preventing cells undergoing progressive necrosis 24–48 h after burn in the zone of stasis [71,72]. All these effects may contribute to prevent progression of damage and reduce scarring [73]. Many studies also focus on the ability of cold water to decrease edema [67,74–76]. However, this mostly seems to be a transient effect and has not been shown to improve the healing of the burn wound. The use of cold water treatment first appeared in St. John Ambulance first aid manuals in 1965 together with the recommendation not to apply any lotions to the burn. By 1969, the recommendation was to irrigate with cold water, followed by cold compresses, and then to cover the wound with a clean/sterile cloth [77]. These continue to be the recommendations prescribed by many organizations today, although many are unclear on the recommended duration of cold water application.

Although most authorities recommend the use of cold water, there is still debate over the best temperature of water to use. Because of the perceived potential for hypothermia after cold treatment, some researchers advocate treating the area with lukewarm or body temperature water, rather than cold water [70]. The use of ice to treat burn injuries has been a contentious issue, with early clinical reports advocating its use, whereas other reports stating that ice can damage tissue or lead to frostbite [64].

3.6. *Values and preferences*

Indigenous/native cultures have developed various nonwater burn treatments which were determined by the availability of local medicinal plants and trees and their natural healing properties [37]. A recent review of four clinical trials investigating the effect of aloe vera on burn wounds found that aloe vera significantly shortened the wound healing time compared to control. The investigators concluded that it may be an effective treatment for first and second degree burns [37,79]. Studies by Cuttle et al. using aloe vera as first aid on a porcine deep dermal burn found that aloe vera-treated wounds were no different from control wounds (treated with nothing) in terms of speed of re-epithelialization, scar formation, or cosmetic appearance [59]. Honey is a natural product that is produced by an insect known as the bee. Honey contains beeswax, berberine, sitosterol and other phytochemicals. Its use for wound dressing either in the natural form or as processed products is well known. The use for first aid in burns, however, is controversial. We are of the opinion that all the various agents used as water alternatives do not satisfy the stated objectives of first aid care [19,37,62].

3.7. *Costs*

Water is obviously the least expensive of all the various agents adopted for cooling. It is also generally available even if it is not running tap water. In RLS, cool potable water at ambient temperature is effective.

Recommendation 4

First aid for chemical injuries should, in addition to first responder safety, include identifying the agent, following specific protocols for the chemical agent if present, removing and disposing of all contaminated clothing and materials while lavaging copiously with water for up to 45 min.

4. Considerations in formulating Recommendation 4

Chemical burn injuries are caused by contact, ingestion, and inhalation of noxious fumes of acids, alkalis or organic materials. A wide variety of chemicals commonly used as industrial and as household cleaners have been identified as having the potential to cause burns [35,79]. Knowledge of the potential harm of these agents in industry is often underestimated and is very inadequate in the domestic setting [79]. Most chemical burns occur on the face, eyes, hands, arms, and legs.

Depending on the extent of the chemical burn, the individual himself/herself or someone close by can administer first aid. First aid givers must wear protective gloves, mask, eye protectors, etc., to avoid making contact with the chemical [79]. First aid measures for chemical burns involve several aspects such as removal of the chemical agent; treatment of the systemic toxicity, if any, and side effects of an agent; general support; special considerations for specific agents if appropriate; and local care of the burn (if it is relevant at this stage, depending on the nature of the chemical involved).

The duration of the chemical's contact with the skin is a major determinant of injury severity as tissue destruction continues as long as the chemical agent is in contact with the tissues [79–82]. As a result, the immediate removal of the agent is very important. This requires removal of involved clothing and a thorough irrigation with water at the scene of the accident. Irrigation should be copious, and to the floor or in a special tank for runoff water, avoiding placing the patient into a tub, which could spread the injurious agent to previously unexposed tissue and increase the damage. Periods of 30 min to 2 h of lavage have been recommended [79].

Although copious water lavage is recommended for virtually all chemical burns, there are a few notable exceptions. Some chemicals create significant an exothermic reaction when combined with water [80]. Phenol is insoluble in water and should first be wiped off the skin with sponges soaked in solubilizing agents such as 50% polyethylene glycol [82–84]. Dry lime contains calcium oxide, which reacts with water to form calcium hydroxide which is an injurious alkali. Therefore, dry lime and other powdery chemicals should be dusted off the skin prior to lavage [85]. Muriatic acid and concentrated sulfuric acid produce extreme heat when combined with water. These agents should be neutralized with soap or limewater before lavage.

4.1. *Balance of benefits and harms*

Neutralization of chemicals has been one of the most controversial points of discussion in chemical burns treatment. Some authors have shown that dilution of the chemical, and not neutralization, is the key point of therapy because it is very efficacious for acid and alkali exposures [78–80]. Neutralizing solutions theoretically should effectively remove the active chemical from a wound and provide relief from further injury, but the control of the quantity of the neutralizing agent is the key difficulty. Problems associated with using neutralizing solutions include exothermic reactions which in turn

cause further thermal damage and delay of hydrotherapy while the neutralizing agent may be sought. It is also important to remember that neutralizing agents can themselves cause toxicity [83,85]. Still, in some cases when the appropriate antidote is known, there is some benefit in its use [86].
The eye is often involved in chemical burns [83]. Even very small volumes of a strong corrosive fluid can produce significant damage to the eye. In these cases an ophthalmologist must be consulted immediately [87–89]. For such injuries it is recommended that irrigation with water must start as soon as possible and be continued for long periods of time (0.5–1 h) [72,83].

4.2. *Values and preferences*

Domestic chemical burns are best treated with copious water as most domestic chemicals are not as corrosive as industrially used chemicals and alternatives (neutralizing agents) are not always available. In an industry setting there are protocols for dealing with a chemical burn. There are also trained responders who might know how to identify the chemical and decide whether a neutralizing agent is available/suitable or lavage with water is the preferred first aid.

4.3. *Costs*

Water is obviously the least expensive of all the various agents adopted for first aid in chemical burns and it is readily available.

Recommendation 5
First aid for electrical injuries should include attending to first responder safety, turning off the electric source or separating the victim from the source with nonconducting material, beginning cardiopulmonary resuscitation (CPR) when necessary, and cooling the burns.

5. Considerations in formulating Recommendation 5

Electrical injuries are uncommon but can be dangerous and deadly not only for patients but also for responders [35,90]. Electrical injuries and burns are a worldwide problem. Electrical injuries are traditionally (and arbitrarily) divided into high-voltage and low-voltage exposures. A high-voltage exposure is defined as exposure to more than 1000 V. A further distinction is made between injuries caused by high-voltage current that has direct contact with the body and those of flash injuries, which are caused by exposure to a high-voltage arc that stretches between the source and the victim [91]. The arc may generate very high temperatures that can ignite clothing, resulting in secondary thermal burns [91]. High-voltage injuries may largely spare the skin surface but cause massive damage to underlying soft tissue and bone [92]. These injuries are also associated with a greater risk for related polytrauma. High-voltage electricity causes muscle tetany leading to the patient's inability to let go of the electrical source. When trauma is associated with electrical burns, trauma life-support measures should be taken.
Low-voltage exposures include common household circuits that provide 120-230 V for general use and for high-power appliances. Low-voltage injuries tend to create small, well-demarcated contact burns at the sites of skin entry and exit. Small children often encounter household electricity. Prevention remains the best treatment of low-voltage electrical burns. Parents should be educated regarding potential safety hazards and the need for close supervision of their children; this is important to decrease the incidence of childhood electrical injuries.
The primary goal during prehospital management of patients with electrical injuries is to secure the scene. The underlying theory presumes that if the victim is still in contact with the electrical source, he or she (or even the ground, if it is wet) can become a conductor and electrocute the rescuer, although no published reports describe this. Before approaching the victim, medical personnel should ensure that the power source has been turned off. Even after this has been done, some "residual electric charge" may still remain with large capacitors and condensers [35]. Therefore, a victim should be removed with a nonconducting material such as a dry wooden stick/pole/wooden chair. Ideally, the first responder must stand on the dry surface during rescue. No such maneuver should be attempted while a person is connected to a high-voltage source, as the current is likely to "arc" to the rescuer as he approaches [35]. Once the scene is safe, prehospital rescuers should focus on administering aggressive and persistent CPR, even if the victim appears to be dead [93].
Lightning is a natural atmospheric electrical discharge that occurs between regions of net positive and net negative electric charges. Lightning burns are often superficial and present with a spidery/arborescent pattern-marking which rapidly disappears. Burns in the region of metallic objects such as a necklace, watches, rings, etc., may also be seen [93]. The victims of lightning injuries are managed in the same way as those of electrical injuries. First aid involves assessment of the level of consciousness and administering immediate CPR at the scene if there is no response. During thunderstorms, one should remain inside a closed car or in a building away from doors and windows; metal objects such as pipes, sinks, radiators; and plugged-in electrical appliances [35]. When outdoors and unable to find shelter, it is important to maintain distance from tall trees. Lightning can travel through water; thus it is important to avoid swimming, boating and bathing during a thunderstorm [35].

5.1. *Balance of benefits and harms*

Electrical burns have usually been more frequent in developing countries with an inefficient electric energy system and a low social and economic level [94]. International data show that electrical injuries account for 5.8% of all burns cases [95–97]. However, developing countries have an electrical burn admission rate between 21% and 27% [98]. The high incidence of electrical burns may be the consequence of the low social and economic level of the population, improperly insulated wires, poorly placed and managed electrical switches, illegal electrical connections, and repair work performed on the electricity grid by nonprofessionals [99]. Education, enforcement and training should be stressed as the primary weapons to combat this problem. Enforcement of existing safety

regulations should be reiterated, and employers should maintain stricter adherence to these regulations. Workers exposed to electric current and electrical equipment should be fully trained/certified and properly dressed. This education/certification will lessen the burden of incurring electrical burns [94].

5.2. *Values and preferences*

These considerations are not applicable to this recommendation.

5.3. *Costs*

Costs associated with this recommendation are not significant.

Recommendation 6
Transfer burn victims to the nearest medical or burn facility. Elevate limbs during transportation in order to limit edema, and position the patient between lying and sitting in suspicion of inhalation burns. If trained personnel are available at the site, clinical assessment should be performed according to the ABCDE method (airway, breathing, circulation, etc.).

6. Considerations in formulating Recommendation 6

Significant burn injuries require transfer to the nearest hospital and subsequently to a burn facility. If transfer is immediately possible and transport time is within 15–20 min, the burn victim can be sent immediately (even without initiating therapy). It is necessary to learn in advance where the patient is to be sent and to calculate the journey time, bearing in mind traffic hold-ups and other possible delays [35]. The ambulance or other transport teams must be informed about the procedures they must observe to ensure continuation of any infusion therapy that has already been initiated.
Any patient receiving a copious lavage to cool the burn wound or adequately dilute chemical exposure is in potential risk for hypothermia. It is important to avoid this complication by maintaining the ambient room temperature between 28 °C and 31 °C. Clinical assessment of the depth and extent of burns should be performed by trained personnel along prescribed trauma guidelines. Fractured, immobilized limbs must be supported in the nonpressure position. It is essential to accompany the patient in transport if there are respiratory problems. Victims with inhalation burns should be propped up and given 100% oxygen as soon as available, even during transport. Conventional thermal burn formulas for resuscitation are used when necessary, including monitoring urine output to assess the adequacy of end organ perfusion and hence resuscitation [100].
After cooling and during transport, the burned body area should be wrapped in a clean, dry sheet/cloth in order to prevent contamination. Wrapping the burn wound minimizes contamination by shielding the wound from secondary infection, reducing pain produced by the exposure of the damaged nerve endings (in partial thickness burns) to the air currents, and providing protection during transport [35]. Plasticized polyvinyl-chloride (PVC) film available as a "cellophane" food-wrap is thought to be a good alternative to cover the burned areas. Little evidence could be found to demonstrate the effectiveness of cling film as a suitable barrier following initial cooling of a burn or scald. However, anecdotal evidence suggests that cling film is a suitable dressing since it is widely available, transparent (enabling subsequent assessment for any signs of infection), and less painful to remove than other dressings, such as gauze [42–44].

6.1. *Balance of benefits and harms*

The primary purpose of any transport team is not to bring a patient to an ICU but to bring that level of care to the patient as soon as possible [100]. Once the need for transport of a burn patient is established, the decision must be rendered concerning what type of transportation vehicle will be used [100]. There are two models of transport commonly used: ground (ambulance/transport vehicle) or air (helicopter, fixed wing), or a combination of both. Factors to be considered when selecting a mode of transportation are the condition of the patient and the distance involved [100]. Ground transport should be considered when covering distances of 70 miles or less. Air transport is used primarily when long distances or the critical nature of an injury separate a team from a patient. Air transport, however, does present its own unique set of problems which must be taken into consideration. In preparing for organizing the transfer of a burn victim, consideration must be given to the continued monitoring and management of the patient during transport [101].

6.2. *Values and preferences*

The main responsibility of prehospital emergency personnel before patient transfer is to rescue the injured victims within a shorter time than the standard. In fact, timely transfer of patients to hospitals is one of the most important principles of prehospital emergency care. In RLS there is limited information about the transport of burn victims to hospitals and the associated factors in real-life environments; therefore, understanding this process and the involved factors is of pivotal importance. Transfer of burn victims can be a challenging experience. Prehospital emergency medical and ambulance services are often poor or non-existent. Roads may just be foot tracks that are not motorable. Risks during patient transfer may therefore manifest in two categories: "jeopardizing the victim's safety" or "jeopardizing the victim's life" [102].
Jeopardizing the victim's safety may occur if the first aid- or emergency medical services (EMS) personnel and burn victims lose their balance while the ambulance is on the move or passing over road bumps. Under such circumstances, considering the restlessness and agitation of burn victims, any intravenous catheter may be detached from the patient and the victim might fall off the stretcher [102].
Jeopardizing the patient's life may derive from challenges such as heavy traffic which leads to delays in the implementation of advanced therapeutic measures for burn victims at the receiving medical facility [102].
In RLS, therefore, the mode of transport should be of appropriate size and have emergency equipment available

as well as trained personnel. This fact also buttresses the need for first aid training in such environments.

6.3. Costs

Transport costs will vary depending on the availability of organized EMS. In RLS, any available transport will serve as long as the aim is to get the victim safely to a medical facility in the shortest possible time.

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Topical agents in burn care

Recommendation 1

A topical antimicrobial agent should be applied to most burn wounds because a burn wound infection may have serious consequences including wound conversion, invasive infection including sepsis, skin graft failure, and prolonged hospitalization. However, many topical antimicrobials are cytotoxic to keratinocytes and fibroblasts and may impair wound healing. Therefore, the choice, concentration, and duration of application of a topical antimicrobial should be based on weighing the risk and consequences of a burn wound infection against the risks of delaying wound healing.

1. Considerations in formulating Recommendation 1

Patients with burns are prone to the development of infections, due to the presence of cutaneous wounds, loss of the barrier function of skin, and the generalized immunosuppression that accompanies a major burn. Approximately 75% of deaths following resuscitation of the burn patient are attributed to an infection [103]. Wound infections are particularly concerning: data from the US National Burn Repository over a 10-year period indicate that wound infection or cellulitis accounted for approximately 20% of 19,000 recorded complications [104].

All burn wounds will eventually become colonized by microbes, although this does not always lead to an adverse event. With sufficient numbers or specific types of pathogens, however, infection of the burn wound may develop, leading to harm. The spectrum of infective microbes is extremely wide and includes gram-positive and gram-negative bacteria (especially *Pseudomonas aeruginosa* and *Acinetobacter* species), multi-drug resistant organisms (MDRO), (such as methicillin-resistant *Staphylococcus aureus*, MRSA), as well as yeasts, fungi, and viruses [105,106].

Burn wound infections are a serious problem that may lead to conversion of the burn wound, delayed healing, skin graft failure, and increased length of hospitalization. Most importantly, invasive burn wound infections lead to septicemia and death [107]. Thus there is a need to control the growth of microbes in burn wounds.

Systemic antimicrobial drugs are not recommended because they are ineffective against colonization and infection of the burn wound [108]. Avascular eschar and the presence of biofilms are the main impediments that limit the usefulness of systemic antimicrobials, and the routine use of these agents only leads to the emergence of potentially dangerous resistant microbial strains. In contrast, topical antimicrobials are delivered directly to the burn wound, and to varying degrees penetrate eschar and limit the development of infection. Consequently, the use of topical antimicrobials has been a major contributing factor to the improvement in outcome following burn injury [107,109,110]. The ideal topical antimicrobial should have a broad spectrum of activity, good ability to penetrate eschar, long duration of action, and low toxicity.

The use and choice of a topical antimicrobial agent has been affected by two important developments. First, deep partial thickness and full thickness burns are surgically excised much earlier now, which limits the duration of topical antimicrobial therapy. Second, it is now recognized that many topical antimicrobial agents are cytotoxic to cells important for wound healing, such as keratinocytes and fibroblasts, and as such have the potential to delay wound healing. Therefore, it is not surprising that in systematic reviews of controlled trials comparing biosynthetic skin substitutes to topical antimicrobial dressings for superficial partial thickness burns, faster healing was observed with the use of skin substitutes [108,111].

1.1. *Balance of benefits and harms*

Infection of the burn wound may have serious consequences, including delayed or compromised wound healing, invasive infection, and sepsis potentially leading to death. Topical antimicrobials limit burn wound infection and are therefore considered beneficial. To varying extents, most of the topical antimicrobials also can delay healing through inhibition of keratinocytes and fibroblasts. Consequently, the choice of a topical antimicrobial agent must be based on a careful

consideration of balance between the risk of a burn wound infection and its adverse outcomes, and the potential risk of impairing wound healing.

1.2. Values and preferences

While most burn practitioners will apply a topical antimicrobial agent to a burn wound, the choice of the agent will depend largely on the depth and extent of the burn and the expected likelihood of developing a burn wound infection, the established practice patterns, the availability of topical agents, and costs.

1.3. Costs

While all topical antimicrobial agents have a financial cost, this must be compared against the potential clinical and financial costs that are incurred when a burn wound becomes infected.

Recommendation 2

Silver-containing compounds and dressings are effective topical antimicrobial agents. However, silver also has cytotoxic effects which may delay wound healing. Silver-based topical agents are quite appropriate for deeper burns and long-acting silver agents are also used on superficial wounds that are expected to heal spontaneously.

2. Considerations in formulating Recommendation 2

Silver has been recognized as an effective topical antimicrobial agent for centuries, and is the basis of established topical antibacterial agents for the burn wound such as silver sulfadiazine (SSD) cream, silver nitrate solution, and silver-releasing dressings. Metallic silver (Ag^0) is biologically inert and has no antimicrobial activity, but the silver cation (Ag^+) is highly reactive, and is lethal to bacteria, yeasts, and fungi in a concentration-dependent fashion, using multiple mechanisms [112–115]. Resistance to silver is quite uncommon, probably because silver acts through several mechanisms, but some evidence suggests that chronic exposure to very low concentrations of ionic silver can induce resistance [116].

Silver nitrate ($AgNO_3$) 0.5% solution has been in use as a topical antimicrobial agent for burn wounds since the mid-1960s. Ionic silver dissociates from $AgNO_3$ to effectively inhibit a broad spectrum of bacteria on the burn wound, including some yeasts. The free silver ion readily precipitates with chloride and any other negatively charged moieties, inactivating the silver and creating inert silver salts. Consequently, silver ions do not penetrate deeply into the eschar, and must be frequently replenished by keeping the gauze dressings on the wound continuously wet with the 0.5% $AgNO_3$ solution. Mortality from invasive burn wound sepsis has been significantly reduced compared to predicted mortality with the use of $AgNO_3$ dressings [117].

Silver sulfadiazine is a water-soluble cream containing 1% SSD. Primarily, SSD's effect arises from a continuous dissociation and deposition of silver ions on the wound surface; the sulfadiazine does not have a major antimicrobial effect. SSD is effective against a wide spectrum of bacteria found in the burn wound, as well as *Candida albicans* and some fungi [118,119]. Retrospective comparative studies in humans with second- and third-degree burns have found that the use of SSD was associated with less bacterial invasion of the burn wound, reduced infection rates and lower mortality [120–122]. Drawbacks of using SSD include cutaneous hypersensitivity to the compound in a minority of patients, and formation of an obscuring pasty yellowish-white exudate (referred to as a "pseudoeschar"), on the wound surface. Finally, SSD has a relatively short duration of action, and penetrates only the superficial part of the burn eschar. In order to preserve a sufficient reservoir of silver on the wound surface, SSD should be reapplied more than once per day, which has implications for patient comfort and for resources [122].

A newer way to continuously deliver silver to the burn wound is with the silver-releasing dressing. The list of currently available silver-releasing dressings is extensive, but the individual dressings can be classified as belonging to one of three groups: nanocrystalline dressings, hydrocolloid or hydrofiber silver dressings, and activated charcoal dressings with silver [113,123,124]. Nanocrystalline silver dressings have demonstrated in vitro activity against a wide variety of common clinically relevant bacteria, antibiotic-resistant organisms, as well as yeasts and fungi [125,126]. A clinical study in burn patients with a mean full thickness burn size of 19.5% total body surface area (TBSA), found that burn wound infections and secondary bacteremia were less frequent in wounds treated with nanocrystalline silver dressings as compared to silver nitrate dressings [127]. However, a more recent Cochrane systematic review concluded that there is insufficient evidence to determine that silver releasing dressings prevent burn wound infections [128]. It should be noted, though, that the review involved predominantly randomized clinical trials of patients with partial thickness burns, where the risk of infection is much lower [128].

Silver's cytotoxicity to keratinocytes was recognized as early as 1965 by Moyer who stated that a 1% concentration of $AgNO_3$ damaged the regenerating epidermis of second-degree burns [117]. Cytotoxicity to keratinocytes and fibroblasts from silver has been demonstrated in a number of in vitro studies, and SSD has exhibited direct cytotoxic effects on keratinocytes and appeared to slow the healing of second-degree burns in vivo [129–133]. The combination of SSD with 0.2% chlorhexidine digluconate (Silvazine) was particularly toxic to keratinocytes in vitro [130]. A prospective study of patients with biopsy-proven second-degree burns found that application of SSD-chlorhexidine significantly slowed healing compared to use of paraffin (tulle gras) dressings alone [134]. A recent systematic review of randomized controlled trials of conservatively treated partial thickness burn wounds that compared SSD to an alternative dressing or topical agent found that use of SSD significantly delayed healing in 28 of 46 studies that reported time to healing [135]. No difference in time to healing was seen in 15 of the 46 trials, while three trials found a statistically insignificant trend toward faster healing when SSD was not used. A Cochrane systematic review of randomized controlled trials examining SSD compared to dressings or skin substitutes for superficial and partial thickness burns found that low-quality evidence identified consistently slower healing with SSD dressings [111]. With respect to the use of nanocrystalline silver dressings, some

studies have demonstrated faster re-epithelialization across meshed split thickness skin graft interstices and partial thickness burns [136,137] while one study found delayed epithelialization of split thickness skin graft donor sites [138].

2.1. Balance of benefits and harms

The main benefit of silver-based topical agents is their effectiveness against a broad spectrum of burn wound pathogens. Infection of the burn wound can lead to invasive infections and sepsis. Infection can also significantly impair wound healing. However, ionic silver also has the potential to delay wound healing because it is toxic to keratinocytes and fibroblasts. Yet translation of these observations on silver efficacy and cytotoxicity from controlled in vitro experiments to the complex environment of the burn wound should be done with caution. Concentrations of free ionic silver may vary widely between wounds and types of silver-containing dressings because Ag^+ is readily bound and inactivated (i.e., "consumed") by a variety of proteins and compounds on the wound surface and in the wound fluid. Thus, the actual clinical potential for silver-based agents to either augment or impede wound healing is unknown at present, and the available literature on the subject is generally of low quality. It is necessary to strike the right balance between obtaining adequate antimicrobial silver concentrations and avoiding silver concentrations that are cytotoxic. In some countries, especially in resource-limited settings (RLS), biosynthetic and biologic dressings for partial thickness wounds are not available, and a short course of SSD may be the most practical alternative to avoid wound infection and its serious consequences.

2.2. Values and preferences

Silver-based topical agents may be preferred for deeper burn wounds where the risk of infection is higher. This would especially apply to the burn wound prior to surgical debridement. Silver-based agents such as SSD and $AgNO_3$ may be less suitable for more superficial burns that are expected to heal on their own, although it is recognized that some long-acting silver-based hydrofiber and activated charcoal silver dressings are widely used for outpatient burn management, especially in children.

2.3. Costs

Prevention of burn wound infection is essential not only for improving outcomes but also for cost containment. However, silver-based topical agents for burns wounds are relatively expensive, and their use should be justified based on the depth of burn and likelihood of infection.

Recommendation 3

Mafenide acetate (MA) is an effective topical antibacterial agent but it lacks antifungal activity. MA's ability to penetrate eschar and tissue make it ideal for deep or infected burns and deep burns of the ear. MA is cytotoxic to keratinocytes and fibroblasts, making it less suitable for superficial burn wounds that are expected to heal spontaneously. Adverse effects from the 11% cream are reduced with the 5% aqueous solution, while addition of topical nystatin may limit the risk of fungal overgrowth.

3. Considerations in formulating Recommendation 3

Mafenide acetate (Sulfamylon®) is a topical bacteriostatic sulfonamide antibiotic that originally appeared in the form of an 11% cream with an osmolarity of 2000 mOsm/L. The agent was primarily intended to combat the problem of invasive gram-negative burn wound infection and septicemia, especially due to *Pseudomonas aeruginosa*. MA is active against many gram-positive and gram-negative bacteria, including anaerobes, but it has poor antifungal activity. For this reason, many practitioners combine it with nystatin. Mafenide is exceptionally good at penetrating deep into eschar and tissue, making it quite useful for application on full thickness, infected burn wounds. The effectiveness of MA cream for the reversal of invasive *Pseudomonas* burn wound infection has been reliably demonstrated in vivo [139]. The introduction of MA cream was also associated with significant reduction in the incidence of invasive burn wound infection and the associated mortality in adult patients with burns between 40% and 79% of the TBSA [107,110]. The ability of MA to penetrate deeply into the wound makes the 11% cream particularly well suited for application to full thickness burns of the ear, to prevent bacterial invasion into the underlying cartilage that can result in suppurative chondritis. This destructive and disfiguring complication has been virtually eliminated by twice daily application of MA cream to the deeply burned ear [140].

Although MA cream is a very effective topical antibacterial agent, it does have some drawbacks. As noted, it has minimal antifungal activity, so wounds repetitively treated with this agent may be prone to fungal overgrowth. It may be quite painful on application, particularly on superficial burns, and this is probably related to its high osmolality and hypertonicity. The agent is also an inhibitor of carbonic anhydrase, so that when MA is repeatedly applied to large surface areas, a metabolic acidemia with compensatory hyperventilation may develop. Absorption of the drug from the cream is rapid, which necessitates re-application of the cream and overlying dressing twice a day. The agent also leaves a thick adherent residue on the wound surface (a "neoeschar," or pseudoeschar), making it difficult to evaluate the wound. As is the case with many other topical antimicrobials and antiseptic agents, MA is also cytotoxic to cells essential for wound healing, such as keratinocytes and fibroblasts. In vitro, MA, varying in concentration from 2.5% to 7.5%, showed dose-dependent toxicity to populations of keratinocytes and fibroblasts [141]. Even at much lower concentrations of 0.85%, MA continued to inhibit keratinocyte growth in vitro [142], and another in vitro study showed that exposure of human fibroblasts to MA at concentrations as low as 0.1% led to cell injury and widespread cell death [133]. A study involving side-by-side comparison of MA and Xeroform® on split thickness skin graft donor sites reported that healing was delayed by the application of MA [143]. Finally, some patients develop a rash, and as with other sulfonamides, MA should not be used in people who are sulfa-allergic.

In some burn centers, to limit the problems associated with MA such as acid-base disturbances, pain on application, and lack of antifungal activity, MA is alternated with silver sulfadiazine during twice-daily dressing changes [110]. An alternative approach, introduced over 20 years ago, was a 5% clear, colorless aqueous solution of MA with an osmolarity of 380 mOsm/L. This was intended to help address the problems of pain on application, acid base disturbances, and production of the obscuring pseudoeschar on the wound surface. The 5% solution has a similar antibacterial spectrum as the cream. A wide variety of multi-drug resistant organisms (MDROs) including methicillin-resistant *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Acinetobacter* species were found to be susceptible to the 5% solution. Addition of nystatin did not affect MA's effectiveness against these MDROs [144]. In vivo studies have found that the 5% solution actually obtained longer and higher peak tissue levels than the cream; the solution achieved more rapid and equally effective bacterial control compared with the cream, and left a cleaner wound surface without an obscuring neoeschar [145,146]. The 5% solution was originally intended for later use in burn wound care, such as on chronic granulating wounds and freshly applied meshed split thickness skin grafts. However, its use has now been expanded to include application in all phases of burn wound care, including initial topical care on the unexcised burn wound and eschar as well as on freshly applied skin grafts [147]. In this role, there were no acid-base disturbances, and discontinuation of the dressing due to pain occurred in only 6% of the subjects. *Candida albicans* colonized 18% of the wounds but was controlled by the addition of 500,000 units of nystatin to each liter of the solution. There were no cases of *Candida* burn wound sepsis or candidemia. The reduced pain on application was attributed to the lower osmolality of the solution, and resulted mainly when the solution was applied to the partial thickness burns. More reliable take of split thickness grafts was observed on wounds that had "borderline" bacterial counts near 10^5 organisms/gm of tissue [147].

Most recently, a 2.5% solution of MA was assessed for its activity against common bacterial isolates such as *Staphylococcus aureus*, *Pseudomonas*, and *Klebsiella* species and was found to be equivalent to a 5% solution. In a recent clinical study [148], the 2.5% MA solution was introduced as an alternative to the 5% solution for immediate application to the burn wound eschar, except if there was sepsis, presence of a MDRO, or suspected/probable silver nitrate failure. There were no significant changes in the incidence of wound infection or bacteremia, and substantial cost savings were realized with substitution of the 2.5% solution. Neither the 2.5% nor the 5% solutions were associated with any side effects.

3.1. *Balance of benefits and harms*

Mafenide acetate's proven benefit as a topical antibacterial for deep or infected burn wounds must be weighed against its lack of antifungal activity, pain on application, promotion of acid-base disturbances, and inhibition of wound healing. To some extent these adverse effects have been ameliorated by the use of the 5% and even the 2.5% solution, and addition of nystatin will help control fungal overgrowth if MA is used over a prolonged period. The major benefit of topical application of the 11% cream to the deeply burned ear in preventing suppurative chondritis greatly outweighs any local adverse effects such as pain on application. Presently there is insufficient evidence to comment on relative benefits and harms of application of 2.5–5% mafenide solution on superficial burns, but in vitro evidence of toxicity to fibroblasts and keratinocytes should be taken into consideration.

3.2. *Values and preferences*

The use of MA will likely be determined by its availability and the established practice patterns within a given burn unit.

3.3. *Costs*

The cost of MA may limit its use in some centers, especially those in RLS. Substitution of the 5% solution with the 2.5% solution may significantly reduce costs and provide equivalent efficacy under most circumstances.

Recommendation 4

Topical antiseptic solutions such as Dakin's solution and acetic acid have broad spectrum antimicrobial effects and rare antimicrobial resistance, and are effective against biofilms, making them useful for chronic, heavily colonized, and infected wounds.

4. Considerations in formulating Recommendation 4

For the purposes of this discussion, an antiseptic agent is a chemical that is applied externally to the surface of a wound to reduce growth of microorganisms. Antiseptics typically act via multiple mechanisms, and microorganisms do not develop resistance to antiseptics as easily or as frequently as they do to antibiotics. Antiseptics are used for clinically infected wounds to slow or halt the spread of infection, but they may also be applied to wounds to prevent the onset of infection.

Hypochlorous solutions have been recognized as effective antiseptic agents for wounds for over a century. Household bleach is a 0.5% solution of unbuffered sodium hypochlorite (NaOCl) that is used to decontaminate surfaces, but it is not meant to be applied to human tissue. In contrast, Dakin's solution is a buffered solution of 0.5% NaOCl. Dakin's solution has been shown in vitro to kill an extensive spectrum of bacteria including MDROs as well as fungi and viruses [149]. To date, no bacterial resistance to NaOCl has been reported. An impressive and recently discovered property of Dakin's solution is that it is also able to disrupt biofilms [149], making the solution an appealing topical antiseptic for chronic wounds. The minimum effective antimicrobial concentration of Dakin's solution is uncertain. One in vitro study found that 0.00025% was effective [141], while another determined that 0.025% was effective against all tested bacterial strains [150]. There are no controlled clinical trials on the use of NaOCl solutions as a topical agent for burns.

Dakin's solution is cytotoxic to keratinocytes and fibroblasts and thus has the capacity to impair wound healing.

Consequently, "half-strength" Dakin's (0.25% NaOCl), and "quarter strength" Dakin's (0.125% NaOCl) have been advocated to reduce toxicity to healthy cells and tissue while still achieving an antiseptic effect. Unfortunately, the literature shows considerable disagreement regarding the concentration of Dakin's solution that causes injury to healthy cells. In vitro studies have reported that toxicity to keratinocytes and fibroblasts occurred with concentrations higher than 0.025% [150], higher than 0.005% [151], and higher than 0.00025% [141]. Another unresolved question is the optimal duration of contact of Dakin's solution on the wound. Solutions of NaOCl act quickly against microorganisms but the effect on the wound surface is short-lived. Recognition of this phenomenon led to the development of the "Carrell" method in which Dakin's solution was continuously delivered to the wound bed. This approach appears to have been abandoned in the modern use of Dakin's, in which gauzes soaked in the solution are applied and changed on the wound only once or twice daily.

Even though Dakin's solution is relatively inexpensive, it may not be widely available in all parts of the world because its production requires addition of a buffer. A South African group has found that unbuffered sodium hypochlorite solution (which is universally available and inexpensive) with a concentration of 0.006% was bactericidal in vitro to *Pseudomonas aeruginosa* and *Staphylococcus aureus*, and caused minimal toxicity to fibroblasts [152].

Acetic acid (AA) is another antiseptic solution that has been applied as a topical antimicrobial agent to wounds, including burns. A few heterogeneous studies involving a limited number of grossly contaminated or infected wounds suggest that 1–5% AA solutions have been effective, but pain, itching and burning of the skin have been reported at the high end of this concentration range. There are no clinical studies of AA in burn patients. One in vitro study found that 3% AA was bactericidal against a broad range of burn wound pathogens [153]. A more recent in vitro study found that 0.3% AA was not only a minimum inhibitory concentration for numerous burn-wound organisms but was also an effective minimum concentration that inhibited biofilm formation by these organisms. A 2.5% AA solution eradicated established biofilms of all tested bacteria [154]. However, as with other antiseptic agents, AA may be harmful to normal cells. In vitro testing of cultured keratinocytes revealed that a 0.25% solution was strongly inhibitory to keratinocyte growth, but dilution to 0.025% was not [142].

Povidone-iodine and chlorhexidine solutions have been used as topical antiseptic agents on burn wounds. Both agents are effective against a wide range of bacteria and fungi. Presently, both agents are most commonly used as soap solutions to clean wounds, especially as a "prep" of the skin and burn wounds prior to surgery. Chlorhexidine diphosphanilate cream has been tested in burn patients but the agent is difficult to apply and painful for the patient at concentrations above 0.5% [155]. Addition of 0.2% chlorhexidine digluconate to silver sulfadiazine was particularly toxic to keratinocytes in vitro [130].

4.1. *Balance of benefits and harms*

While Dakin's solution is an effective topical antimicrobial solution, it is unknown at present whether it offers any benefit. Most importantly, the ideal concentration at which Dakin's provides an acceptable balance between microbial killing and cytotoxicity is unknown, as is the role of continuous versus intermittent application. Nevertheless, Dakin's solutions may have a role as a topical antimicrobial for deeper burn wounds (that are not expected to heal spontaneously) prior to surgical excision, and for chronic contaminated or infected wounds, especially those with a biofilm. Conversely, Dakin's solution may not be ideal for wounds attempting to spontaneously re-epithelialize (e.g., partial thickness burns and fresh meshed skin grafts) because of its toxicity to keratinocytes.

Insufficient information supports the use of topical AA solutions on burn wounds. The limited data suggest that AA might be beneficial as an antiseptic for infected or heavily contaminated wounds, using a concentration of 2.5%. Caution should be used if AA is being considered for a wound attempting to epithelialize spontaneously (such as a superficial partial thickness burn or a freshly applied meshed skin graft) because of the potential of AA to inhibit keratinocyte turnover.

At present there are insufficient data to make specific recommendations regarding benefits and harms of chlorhexidine and povidone-iodine as topical agents for burn wounds.

4.2. *Values and preferences*

Antiseptic solutions such as Dakin's solution and AA may be preferred options for topical antimicrobial control of deep burns, especially in the absence of more conventional antimicrobial strategies such as silver-based agents or MA. It may be preferable to use these agents on chronic and/or infected wounds that arise in burn care (e.g., due to skin graft failure), especially if a biofilm is suspected.

4.3. *Costs*

Antiseptic solutions such as Dakin's and AA are relatively inexpensive and may be very useful in RLS. Since the buffered Dakin's solution may not be universally available in many parts of the world, the use of 0.006% unbuffered sodium hypochlorite solution may be an economical and beneficial approach.

Recommendation 5

Topical antibiotic ointments provide limited antibacterial coverage as well as a moist healing environment, and may be suitable for small superficial burns including superficial burns to the face.

5. Considerations in formulating Recommendation 5

For the purposes of this discussion, antibiotic ointments are water-in-oil emulsions containing an antibiotic, where the volume of oil exceeds the volume of water. Thus, these agents provide the additional benefit of maintaining a moist wound environment. These agents are believed to promote epithelialization while providing limited control of bacterial flora on the wound surface.

Bacitracin is effective against gram-positive cocci but not gram-negative bacteria or yeasts. Polymyxin B sulfate is active

against gram-negative bacilli such as *Pseudomonas* but it has poor activity against gram-positive species. Neomycin is a topical aminoglycoside ointment that is effective against gram-negative bacilli and some gram-positive species. To overcome the limited spectra of these individual agents, antimicrobial ointments that combine several antibiotics are available. Polysporin combines bacitracin and polymyxin B sulphate while Neosporin® combines bacitracin, polymyxin B sulphate and neomycin. Mupirocin ointment is effective against MRSA [156].

Evidence is limited regarding the ability of these agents to prevent burn wound infection or regarding their effect on healing. Optimal use of all of these agents involves regular removal and wound cleansing, and then re-application two to three times a day, which may be painful for the patient.

5.1. *Balance of benefits and harms*

The benefits of using antimicrobial ointments over other treatment approaches have not been evaluated. The use of topical antimicrobial ointments for small superficial burns carries little risk other than that of allergic and cutaneous hypersensitivity reactions. The exception to this would be application of polymyxin B sulphate or neomycin to very large surface areas which could result in systemic absorption and complications including neurotoxicity, renal toxicity, and ototoxicity.

5.2. *Values and preferences*

Topical antimicrobial ointments are commonly prescribed for small superficial burns in the outpatient setting. They are also commonly used for superficial burns to the face. These agents may be preferred for small superficial burns that will heal by re-epithelialization over silver-based agents, MA, and topical antiseptics, all of which exert some degree of cytotoxicity to keratinocytes.

5.3. *Costs*

All of these agents incur a financial cost, but this should be limited by appropriate restriction of their use to small burn wounds.

Recommendation 6

Topical honey may be considered for use in superficial partial thickness burns, especially in resource-limited settings in the absence of conventional topical antimicrobial ointments and creams. Further study on honey's effects on healing and control of infection is required because of the low quality of existing evidence regarding topical honey on burn wounds.

6. Considerations in formulating Recommendation 6

Honey is a viscous, hyperosmolar and supersaturated sugar compound containing approximately 40% fructose, 30% glucose, 20% water, 5% sucrose, and a mixture of other components including amino acids, vitamins, minerals, and enzymes [157]. Topical honey has been used in wound care since 2000 BC, and more recently the use of topical honey for burns has engaged increasing interest. The effectiveness from applying honey to wounds is incompletely understood but appears to be based on its antibacterial effects (related to hyperosmolarity and peroxide activity), and some evidence in vivo that it accelerates wound healing [158].

A recent systematic review has examined the use of honey as a topical treatment for burns [158]. A total of 11 randomized controlled trials were identified, but it should be noted that the study populations, depths of burns, comparators to honey, and dressing regimens were heterogeneous across these investigations. Furthermore, many of the studies were identified as having either unclear or high risk of selection, performance, and detection biases. Most patients studied had superficial burns that included first- and second-degree injuries.

Two studies involving a total of 992 patients with partial thickness burns compared unprocessed honey application to a variety of other dressing approaches which included polyurethane film (OpSite®), paraffin gauze, sterile linen, antimicrobial gauze (Soframycin® gauze), or exposure. Although both studies were unblinded and both had an unclear risk of selection bias, the evidence regarding time to healing was rated as "high quality" by the Cochrane review, and a pooled fixed-effect model showed that burns treated with honey healed more quickly by 4.68 days (95% CI: 4.28–5.09 days) [158].

Topical unprocessed honey was compared to SSD in six trials. Among the four trials involving patients with superficial burns (ranging from first-degree to deep second-degree) that reported a mean time to healing, very low quality evidence from a pooled fixed-effect model found healing time with honey was reduced by 5.12 days (95% CI: 0.73–9.51 days) compared to SSD dressings [158].

6.1. *Balance of benefits and harms*

Topical honey appears to have novel antimicrobial and stimulatory wound healing properties. However, these potential benefits for burn wounds are difficult to confirm due to considerable heterogeneity between available studies and the overall low quality of most of the evidence. Potential harms and adverse effects related to honey are even less certain. Compared to approaches such as the use of polyurethane films, paraffin gauze, sterile linen, or open treatment for superficial burns (first-degree and superficial partial thickness), no clear association was made between honey and adverse effects such as hypergranulation, scarring, contractures and infection; but again, the evidence is low to very low quality [158]. Compared to the use of SSD, the quality of evidence on adverse effects with honey is better, and suggests significantly fewer adverse effects with honey [158].

6.2. *Values and preferences*

In the absence of more conventional topical antimicrobial ointments, solutions or creams, topical honey may be preferable to wound management approaches such as the use of polyurethane films, paraffin gauze, sterile linen, or open treatment for superficial burns (first-degree and superficial partial thickness).

6.3. Costs

At present, insufficient evidence allows specifying whether topical honey offers a cost savings compared to other topical wound management approaches. Only one randomized controlled trial has examined cost, and that study found that the standardized unit cost of honey per % TBSA of application was much less expensive than that of SSD [159].

Recommendation 7
Cerium nitrate should be considered as a topical agent for full thickness burns when early surgical excision and wound closure cannot be performed.

7. Considerations in formulating Recommendation 7

Cerium is a rare earth element that can form salts with various compounds. Use of topical cerium nitrate (CN) has been of major interest to the burn care community since Monafo's observations on reduced burn wound infection and mortality connected with the use of this agent [160]. While CN solution was originally used as an immersion bath or gauze-soaking solution for burn patients, it has predominantly been applied as a cream that combines 2.2% CN with 1% SSD. Initially it was believed that CN exerted a bacteriostatic effect, but more recent investigations indicate that CN has incomplete activity against common burn wound pathogens, and that addition of SSD does not confer any supplementary antimicrobial effect [161,162]. Rather, CN's main effect appears to be related to its ability to bind and inactivate lipid protein complex (LPC) which is formed when heat polymerizes skin proteins. LPC from the burn eschar has harmful immunosuppressive and pro-inflammatory effects. A second and probably complementary mechanism of action is that application of CN to eschar results in the eschar becoming hard, dry, and firmly adhered to the wound. Thus, the cerium-hardened eschar may act as an impervious protective "shell" that prevents exogenous microbial colonization and infection of the wound, which reduces the likelihood of invasive infection and sepsis. The eschar can remain adhered to the wound for many weeks, with little evidence of sub-eschar infection or eschar separation. At surgical excision the wound bed is typically clean, with minimal granulation, and ready for skin grafting [162,163]. Thus the cerium-treated eschar functions much like a temporary biologic dressing, with the added ability to systemically limit LPC dissemination.

Clinical studies over a 7-year period by Monafo and colleagues, in burned children and adults, found that application of CN-SSD, while delaying excision of the eschar for up to 3 weeks in some cases, was associated with significant improvement in survival compared to historical or predicted mortality rates [164,165]. However, a randomized controlled trial by Munster et al. involving 60 patients with >10% TBSA burns compared SSD to CN-SSD and found no significant difference in sepsis-related or all-cause mortality [166]. Another randomized controlled trial comparing SSD to CN-SSD found that mortality and burn wound colonization were higher in the cerium-treated subjects although this study may have been confounded by a baseline imbalance in the study populations, with older and more extensively burned subjects in the cerium arm [167]. More recent studies suggest that children and the elderly may benefit from more conservative therapy with CN by delaying the first operation until the patient is more stable [168].

7.1. Balance of benefits and harms

Early surgical excision and closure of deep partial thickness and full thickness burns is recommended to shorten time to healing, reduce length of hospitalization, reduce scarring and contractures, and increase survival. Inability to perform early surgical excision is therefore undesirable. However, when early surgical excision cannot be performed, topical application of CN may provide the benefit of creating an adherent, closed biologic dressing that can be safely left intact for weeks while awaiting definitive surgical excision. Adverse effects from CN application are uncommon, with pain on application being the most common problem [162].

7.2. Values and preferences

The need for CN has been supplanted by early surgical excision, which is the current standard of care for deep partial thickness and full thickness burns in facilities that have available resources and expertise. However, in situations where early excision of deep burns cannot be performed or must be delayed, there may be a role for application of CN-SSD. Examples of this would include patients with full thickness burns in RLS where access to early surgical excision and wound closure is unavailable. Another situation would be mass burn-casualty situations where early burn excision and closure may not be feasible due to an overwhelming number of cases.

7.3. Costs

The costs of providing early surgical excision and wound closure are significant and are related to the need for suitable facilities and equipment; frequently the use of temporary skin substitutes, blood transfusion, surgical and anaesthesiology expertise; and postoperative care capacities. Use of CN may potentially be an inexpensive way to safely defer early surgical excision and wound closure, allowing some of the associated costs to be reduced or redistributed. For example, in a resource-limited scenario, a patient with a large full thickness burn and limited autograft sites who would normally require use of expensive temporary or semipermanent skin substitutes (e.g., allograft or dermal replacement templates) to facilitate early excision, could potentially be safely managed with topical CN to allow multiple delayed, staged, and smaller debridements with immediate autograft applications.

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Infections in burns: Part 1—Sepsis

Recommendation 1

Sepsis in the burn patient should be considered differently than sepsis in the non-burn general population.

1. Considerations in formulating Recommendation 1

Multiple differences characterize sepsis in the general population versus that in burn patients [169]. Septic patients from the general population present either to the emergency department or from a medical/surgical ward with a systemic response to a new infection. The primary diagnosis, therefore, is sepsis, and the focus of treatment is to rapidly eliminate the infection. Many efforts to develop accurate definitions of sepsis [170] and standards of rapid treatments [171–173] have been made. Recently, the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) met to streamline and standardize definitions [174–176]. The Surviving Sepsis Campaign was designed to create guidelines for rapid recognition of sepsis and to develop "bundles" for prompt treatment strategies for sepsis and septic shock [171–173]. These efforts have led to the creation of standards for the treatment of all forms of sepsis, but burns have always been excluded from these efforts.

There are several reasons why burns are excluded from the major sepsis and septic shock standards. First and foremost, burn patients lose their primary barrier to microbial invasion, their skin. The initial response to the loss of skin is a profound systemic capillary leak syndrome that we know as burn shock. With any burn greater than 20% total burn surface area (TBSA) the patient soon develops a persistent hypermetabolic response that leads to continuous catecholamine release. The burn patient thus resets his/her set temperature to greater than 38°C, and develops baseline tachycardia and tachypnea. The hypermetabolic state also leads to a tendency toward leukocytosis. All of these findings in the non-burn population are used for triggers for the diagnosis of the systemic inflammatory response syndrome (SIRS). In the patient with a sizeable burn this inflammatory state is routine. Therefore, in the 2007 Consensus of the American Burn Association (ABA), all patients with burns greater than 20% TBSA are considered to have SIRS "by definition" [177]. Clearly, different definitions are required for burn patients.

Unlike sepsis in the general population, sepsis in burn patients occurs later in their hospital stay. Sepsis rarely occurs before one week post burn and it may occur months into the

hospitalization. The prolonged risk for burn patients arises for several reasons. As long as the wound remains open there is persistent source of inflammatory stimuli. Any major burn leads to marked immunosuppression that predisposes the patient to infections with unusual organisms such as fungi and viruses [178]. In addition, during the prolonged hospitalization, the type of organisms that dominates the patient shifts from gram-positive to gram-negative bacteria, to yeast or fungi, and multi-drug resistant organisms (MDRO) often appear. Burn patients also require prolonged exposure to invasive devices—central lines, Foley catheters, and tracheal tubes—that predispose them to higher risks for infection. Clearly, the definition of sepsis in the burn patient is markedly different than that for the general population.

1.1. *Balance of benefits and harms*

The benefit of recognizing different criteria for sepsis in burn patients as compared to other patients is that fewer burn patients will be treated with antibiotics unnecessarily. A great benefit to all patients will be that selective antimicrobial use will reduce the incidence of organisms with multi-drug resistance. The concept of antibiotic stewardship has been a major thrust in many countries with the goal of reducing the increasing incidence of antibiotic resistance [179]. The only potential harm in this policy is that no definition of sepsis will necessarily be applicable to every patient. Continuous vigilance and clinical judgment will be required to identify and treat sepsis.

1.2. *Values and preferences*

The concept of considering burn patients as a unique patient population should become the policy of all burn centers. Patients with small burns (i.e., <15% TBSA) may not have a systemic response and clinical judgment will be required to determine if the patient physiology is best served by the burn sepsis criteria.

1.3. *Costs*

Treating burn sepsis differently than sepsis in the general population will likely reduce total costs for each burn unit by decreasing the number of cultures obtained as well as reducing antibiotic administration. In addition, the increased selection will likely reduce MDRO and will have an even more profound impact on reducing medical costs.

Recommendation 2

All patients with burns greater than 15–20% TBSA should be continuously monitored for subtle signs of sepsis. The diagnosis of sepsis is based on more extreme signs than it is in the general population. Criteria to diagnose sepsis include: higher temperature, lower temperature, greater tachycardia, greater tachypnea, confusion, hemodynamic instability, vasopressor requirements, increased fluid requirements, thrombocytopenia, base deficit, hyperglycemia (insulin resistance), and nutritional intolerance. In addition, a culture-positive infection, pathologic source of infection, or clinical response to antimicrobials is required to diagnose sepsis.

2. Considerations in formulating Recommendation 2

Few efforts have been made to publish a clear identification of criteria to diagnose sepsis in the burn population. The first attempt to define sepsis was spearheaded by the American Burn Association Consensus Conference to Define Sepsis and Infection in Burns [177]. Multiple members of the ABA met in 2007 after reviewing the literature about sepsis and infections. The group then identified the following list of criteria.
Sepsis—the presence of three or more of the following:

Temperature >39°C or <36.5°C
Progressive tachycardia >110 beats/min
(Children >2 standard deviations above age-specific norms)
Progressive tachypnea >25 breaths/min or minute ventilation >12 L/min

(Children >2 standard deviations above age-specific norms)

Thrombocytopenia <100,000/mcL (does not apply until 3 days after burn)

(Children <2 standard deviations above age-specific norms)

Hyperglycemia in the absence of pre-existing diabetes mellitus
(Untreated plasma glucose >200 mg/dl or intravenous insulin >7 units/h IV, significant resistance to insulin [>25% increase in insulin requirements over 24 h])
Inability to continue enteral feedings >24 h
(Abdominal distension, enteral feeding intolerance [two times feeding rate], uncontrollable diarrhea [>2500 mL/day])
(Children enteral feeding intolerance >150 mL/h, diarrhea >400 mL/day)

In addition, a documented infection must be identified, defined as:

Culture-positive infection, or
Identified pathologic tissue source, or
Clinical response to antimicrobials

The ABA Consensus definitions have recently been challenged and need to be scrutinized. Any guideline needs to be tested and updated based on available data. The group from Texas compared the ABA Consensus criteria to findings obtained 3 days prior to signs of a positive blood culture. They identified the following criteria for sepsis [180]:

Heart rate >130 beats/min
Mean arterial pressure <60 mmHg
Base deficit <−6 mEq/L
Temperature <36°C
Use of vasoactive medications
Glucose >150 mg/dL

Furthermore, the group from Loyola University in Chicago, Illinois, reviewed burn patients who were given the diagnosis

of sepsis based on retrospective International Classification of Diseases, ninth revision (ICD9), diagnoses and found that in addition to the ICD9 diagnosis, hyperglycemia facilitated the sepsis diagnosis [181]. This study relied on a previous diagnosis of sepsis in a retrospective manner and would not help a clinician with the future diagnosis of sepsis in an inpatient.

For the diagnosis of septic shock, sepsis is combined with shock-like parameters such as hypotension and the use of vasopressors. The ABA Consensus group used the same hemodynamic parameters defined by the 2004 Surviving Sepsis Campaign [171].

2.1. *Balance of benefits and harms*

Close monitoring of the subtle signs of new-onset sepsis will lead to better patient outcomes. Recent studies demonstrate that more rapid administration of antibiotics decreases mortality [182,183]. The major benefit is thus source control with decreased antimicrobial resistance. However, in resource-limited settings (RLS), achieving timely culture results may not be possible, and in some instances even the evaluation of infection via cultures may be limited. In those cases of infection, clinical judgment must guide treatment.

2.2. *Values and preferences*

In any burn center, it is easy and inexpensive to encourage the practice of closely monitoring patients for sepsis. Resource-limited settings may have limited access to culture supplies and may need to rely in part on clinical judgment to identify and treat infection. Nonetheless, burn centers should have the ability to perform microbiologic testing of blood, urine, wounds, and respiratory secretions. No current evidence supports the use of more advanced tests to determine the diagnosis of sepsis.

2.3. *Costs*

Basic monitoring of changes in vital signs, urine output and simple laboratory values is not expensive. Microbiologic testing and culture sensitivities should be available in facilities taking care of burn patients. The benefits of adding advanced testing (such as polymerase chain reaction), although potentially helpful, remain unproven, and each burn center should evaluate the utility of these tests in the particular environment.

Recommendation 3

Rapid recognition and aggressive empiric treatment of sepsis should improve outcomes in burn patients.

1. ***IV fluids should be provided to a target mean arterial pressure of 65 mmHg.***
2. ***Crystalloids should be the initial fluid, but the role of albumin is not known.***
3. ***The goal is to normalize lactate levels.***
4. ***The vasopressor of choice is norepinephrine with vasopressin or epinephrine as second choices.***
5. ***Dobutamine is an option for inotropic support.***
6. ***Cultures should be obtained (blood, urine, sputum) and the burn wound checked (and cultured if suspected to be infected) prior to starting antibiotics.***
7. ***Empiric antibiotics that cover likely pathogens should be started as soon as possible after the diagnosis of sepsis is made.***
8. ***Consider source control to assist with treating the infection:***
   a. ***Consider excising burn wounds and applying biologic coverage.***
   b. ***Invasive devices such as central lines and urinary catheters should be removed if possible or changed if needed.***

3. Considerations in formulating Recommendation 3

The Surviving Sepsis Campaign efforts clearly establish that early diagnosis and rapid initiation of “sepsis bundles” of treatment improves the outcomes in all forms of sepsis [173,182,183]. While burns have not been addressed in these efforts, the principles of the Surviving Sepsis Campaign are likely to benefit the burn population. Once sepsis is diagnosed, empiric treatment should be initiated as rapidly as possible. The Surviving Sepsis Campaign has developed bundles of several tasks to be completed within a short time period (usually 3 h). There are no bundles described for burn patients, but many of the same principles can be applied. Once sepsis is diagnosed, rapid initiation of resuscitation is essential. The Surviving Sepsis Campaign suggests that the patient should be given 30 mL/kg of IV crystalloid within 3 h and further evaluation of the hemodynamic status should then be completed. As the initial treatment of shock in burn sepsis, this recommendation and the following are relevant. The target should be to obtain a mean arterial pressure of 65 mmHg with fluids or vasopressors, the aim being to lower lactate levels to normal levels. The vasopressor of choice is norepinephrine, with vasopressin or epinephrine being the next alternatives. If inotropic support is necessary, dobutamine is the best choice. The Surviving Sepsis Campaign also suggests further fluid challenges, initially using balanced crystalloids or saline. They also suggest that adding albumin may be helpful when patients require large fluid volumes. These suggestions are also relevant for burns, but the type of fluid still needs to be determined.

The other key point of the Surviving Sepsis Campaign that applies to burns is that empiric antibiotics that cover the likely pathogens should be started within 1 h of diagnosis of sepsis. Prior to the initiation of antibiotics, it is essential that cultures be obtained from the blood, urine and lungs. For burns, the wound should be examined to seek signs of wound infection and if the wound is thought to be infected, it should be cultured. As with all infections, “source control” should be considered, which for a burn patient includes excision of the burn wound with some form of biologic coverage. In addition, if possible, invasive devices should be removed or changed.

3.1. *Balance of benefits and harms*

Multiple studies demonstrate that the shorter the duration between infection diagnosis and treatment, the lower the

mortality [182,183]. Broad-spectrum antibiotics that are likely to treat the source of infection should be initiated. Delay in treatment is likely to increase the risks for complications and death. Other adjunctive treatments, including crystalloid resuscitation, also reduce mortality by improving hemodynamic status. The major risks of empiric therapy are incorrect diagnosis and/or inappropriate resuscitative efforts. While the guidelines provide options for resuscitation, clinical judgment will need to be used to optimize resuscitation, particularly when balancing fluid administration and vasoactive agent use.

3.2. *Values and preferences*

To optimize rapid treatment of sepsis, the burn center should identify the likely infective organisms and the appropriate antibiotics that cover those organisms. The exact resuscitative regimen will vary based on resource availability (i.e., a given hospital may only have a limited selection of antibiotics and/or vasoactive agents). Some environments may have restrictions on operating room availability.

3.3. *Costs*

Since empiric treatment reduces complications and mortality, rapid treatment of shock and initiation of antibiotics known to treat likely organisms will likely reduce overall sepsis costs while optimizing patient survival. However, the cost incurred by initiating resuscitation and antimicrobial therapy will need to be considered.

Recommendation 4
Antimicrobial coverage should be narrowed once a pathogen is identified and sensitivities to antimicrobials are obtained.

4. Considerations in formulating Recommendation 4

Burn patients are frequently colonized with and often infected with highly resistant organisms. The reasons for these resistant organisms are multifactorial. The major reason is that with loss of skin there is prolonged exposure to invasive organisms. Any antimicrobial treatment, whether topical or systemic, creates resistant organisms. Inappropriate treatment with ineffective antimicrobials prolongs infections and potentiates resistance. Once the offending organism is found there is no need to continue antibiotics against other classes of microorganisms since doing so will encourage further resistance to the uninvolved microorganisms. Once sensitivities are determined, focused treatment of that organism with the most appropriate antimicrobial will increase the chances of a successful outcome and reduce the chances of creating more resistance.

4.1. *Balance of benefits and harms*

Rapid adjustment of antibiotics to respond to culture results should also benefit the patient. If antibiotics are not narrowed based on culture results, antibiotic resistance will increase. Prolonged treatment of ineffective and inappropriate antibiotics will simply increase MDRO. It should be remembered, however, that no test is perfect, including antimicrobial testing. Clinicians should maintain vigilance in evaluating patients to avoid missing infection in an untested site and to identify new developing infections.

4.2. *Values and preferences*

All burn centers should develop policies that address the narrowing of antibiotics to properly treat infections. The ability of burn centers to rapidly diagnose infections may be limited by local resources. Hence, each center should work to optimize the accuracy and timeliness of microbial testing so that it is available 24 h/day, 7 days/week.

4.3. *Costs*

Clearly, reducing antibiotics to cover the target organism will reduce costs for that patient and ultimately, reduce the costs of MDRO. The major costs incurred will be for microbial testing and antibiotic administration as well as for personnel to perform the testing and administer antibiotics.

Recommendation 5
Prophylactic systemic antibiotics do not reduce sepsis and should be avoided.

5. Considerations in formulating Recommendation 5

As mentioned with recommendation 4, a high incidence of resistant organisms affects burn patients. The use of prophylactic systemic antimicrobials has never been shown to reduce infections or sepsis [184,185]; it will increase the incidence of multiply resistant organisms in the patient and within the unit.

5.1. *Balance of benefits and harms*

Treating all burn patients with prophylactic systemic antibiotics offers no benefit. Studies from decades ago demonstrated that practicing from this philosophy increases bacterial resistance [184,185]. The resultant increase in MDRO presents a clear harm to both the treated patient and all future patients. Systemic antibiotics may be appropriate in burns that present late (i.e., in patients who present >7 days after injury with signs and symptoms of infection). In these cases, clinical judgment should be applied and cultures obtained to determine if an infection exists.

5.2. *Values and preferences*

Prophylactic antibiotic treatment of burn patients as a policy should be abandoned. In some cultures, the use of prophylactic antimicrobials has become commonplace. However, these preferences contradict good patient care. The exception would be for patients who present late after injury (i.e., >7 days) with clinical signs of infection. In those cases, clinical judgment will need to be employed.

5.3. Costs

The avoidance of prophylactic antibiotics will reduce costs for each patient. That is, in general, reducing drug resistant organisms will also reduce costs to all patients. The major costs incurred are related to microbial testing and antibiotic administration.

Recommendation 6
Efforts to establish the best treatment of burn-related sepsis still poses many unanswered questions. Further study is greatly needed to identify optimal treatment.

6. Considerations in formulating Recommendation 6

Many practices used in treating sepsis have never been proven and may or may not be of value. There is no consensus as to the best method of early diagnosis and early treatment bundles for burn patients. Clearly, criteria for diagnosis and early treatment need to be developed and tested. Other questions that need answers are:

1. Are there early diagnostic tests, such as that for C-reactive protein, procalcitonin, or others, that predict sepsis?
2. What are the effects of using topical antimicrobials?
3. What is the optimal resuscitation fluid for sepsis?
4. Should steroids be given in burn sepsis?
5. What are the effects of using blood products, immunoglobulins, plasmapheresis, renal replacement therapy, anticoagulation, sedation, glucose control, bicarbonate therapy, stress ulcer prophylaxis, and other adjuncts when treating sepsis?

6.1. Balance of benefits and harms

Studies that prove the effectiveness of a modality in treating all infections will benefit all burn patients by decreasing mortality and antibiotic use. Unfortunately, the development and demonstration of efficacy of new modes of treatment will incur costs, restricting its application in RLS.

6.2. Values and preferences

Studies investigating means of optimizing the treatment of burn infections are greatly needed. Because different cultures have different thresholds for developing and applying new testing methods, the application of new testing paradigms depends on local resources and cultures.

6.3. Costs

While the initial costs of investigations, especially multi-center studies, to help determine the best care of burn infection are expensive, the ultimate benefit will be great. Reducing diagnostic tests and treatments that are ineffective will ultimately benefit all burn centers. Each center needs to evaluate methodology currently available and identify areas for improvement.

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Infections in burns: Part 2—Pneumonia

Recommendation 1

Intubated burn patients with either inhalation injury or burns ≥15–20% are at significant risk of, and should be monitored closely for, signs of pneumonia.

1. Considerations in formulating Recommendation 1

Mechanically ventilated burn patients develop pneumonia at rates of up to 65% [186,187]. The increased pneumonia risk in burn patients is multifactorial. First, patients with major burn injury (>20% total burn surface area, TBSA) have a marked abrogation in T- and B-cell function, leading to immunosuppression. Second, inhalation injury, which increases burn mortality, impairs the physical defenses by means such as cilia damage, surfactant impairment, cast formation, and bronchiole obstruction. As a result, inhalation injury increases pneumonia rates to almost 20% in burn patients [188,189]. Pneumonia and infection-related ventilator associated complications (IVAC) have been associated with longer hospital and intensive care unit (ICU) length of stay and ventilator days [190]. IVAC is defined as a sustained increase (2 or more days) in oxygen requirement of >20% over baseline and an increase in positive end-expiratory pressure (PEEP) >3cm water with an associated temperature >38°C or <36°C or a white blood cell (WBC) count >12,000 or <4000 *and* associated administration of an antimicrobial for >4 days.

Burn patients at risk for pneumonia include those with inhalation injury with grade 3 or 4 injury on bronchoscopy, larger burns (>20% TBSA), initial PaO_2/FiO_2 <300mmHg, carboxyhemoglobin >10% on admission, and a history of smoking [191]. The *clinical diagnosis* of pneumonia in burn patients includes two of the following:

(1) Chest x-ray with a new and persistent infiltrate, consolidation, or cavitation;
(2) sepsis (as defined in the section on Sepsis, p. xx);
(3) recent change in sputum or purulence in the sputum [192].

It should be remembered that multiple other diagnoses, such as acute respiratory distress syndrome (ARDS), tracheobronchitis, and chest contusion, may mimic pneumonia. Microbiologic data may modify the diagnosis into one of three categories:

(1) Confirmed: clinical signs and pathogen isolated;
(2) Probable: clinically present without microbiologic confirmation; and
(3) Possible: abnormal chest X-ray with uncertain cause and with low or moderate clinical suspicion, but microbiologic definite criteria met or pathogen identified.

Positive microbiology is defined as tracheal aspirate with $\geq 10^5$ organisms, bronchoalveolar lavage ≥104 organisms, and protected bronchial brush $\geq 10^3$ organisms. It should be remembered that the burn wound can be the source of pathogen spread.

1.1. *Balance of benefits and harms*

Given the high incidence of pneumonia in intubated burn patients, close monitoring for pneumonia carries a far greater potential benefit than risk. Early identification and treatment of pneumonia reduces patient morbidity and mortality.

1.2. *Values and preferences*

Intubation rates in resource-limited settings (RLS) may be lower than in centers with abundant resources. As such, monitoring for pneumonia may need to extend to any patient with a risk of airway compromise regardless of intubation status. The extent and methodology used to monitor patients for pneumonia will be dictated by local resource availability, such as radiology access, culture capability, and bronchoscopy access.

1.3. *Costs*

In general, monitoring patient vital signs and secretions incurs a low cost and can be accomplished in most settings. More advanced studies, such as X-rays and computed tomography scans, and repeated bronchoscopy, may be problematic for RLS.

Recommendation 2

Prophylactic antibiotics do not prevent pneumonia and are not indicated in burn patients on admission even in the presence of inhalation injury.

2. Considerations in formulating Recommendation 2

Only limited studies and no prospective randomized trials demonstrate the utility of administering antibiotics for the prevention of pneumonia at the time of admission to a burn unit. Several meta-analyses have demonstrated that prophylactic antibiotic administration after major burn injury increases the risk of developing resistant microorganisms by changing the resident microflora [193,194]. Data from current available literature provide the basis for the recommendation that antibiotics be reserved for treatment of infections.

2.1. *Balance of benefits and harms*

Antibiotics can be life-saving in treating active infections. However, misuse of antibiotics results in the development of antimicrobial resistance, drug reactions, and prolonged

hospital length of stay. In general, the drug with the narrowest spectrum that is effective against a microorganism should be chosen in established infections.

2.2. Values and preferences

Different settings will have different antibiotic availabilities and different methods of drug administration. Hence, antibiotic use will differ among countries. Antibiotics should be tailored based on culture results and local microbiograms, if available. In cases of delayed excision, which increases burn infection rates, antibiotic administration may be necessary to combat infection.

2.3. Costs

Antibiotic use is associated with a variety of costs, including drug cost, administration and monitoring costs, and costs associated with development of drug resistance. These costs will vary among countries and resource settings.

Recommendation 3
In intubated patients bronchoalveolar lavage (BAL) or subglottic specimens should be used, if resources permit, to obtain diagnostic samples for pneumonia microbiologic diagnosis.

3. Considerations in formulating Recommendation 3

Targeted antimicrobial therapy is a cornerstone in the treatment of pneumonia, particularly in the burn patient, who is immunosuppressed and at high risk for ventilator-associated pneumonia (VAP). In burn patients, BAL has been shown to be equivalent to a protected bronchial brush specimen in the diagnosis of pneumonia [195]. It is important, however, to assimilate BAL findings into the overall clinical context to avoid over- or undertreatment of infection. Likewise, evidence in the surgical literature supports the use of serial catheter-directed BAL in guiding the management of pneumonia in intubated patients [196].

3.1. Balance of benefits and harms

Both BAL and subglottic suctioning can be beneficial in the diagnosis and treatment of pneumonia in intubated burn patients; however, this benefit should be weighed against the risk of complications from the procedures, including pneumothorax, acute respiratory decompensation, nondiagnostic specimen, and loss of airway.

3.2. Values and preferences

Bronchoscopy and subglottic suction devices may not be available in all centers due to resource limitations, lack of equipment, or inability to process specimens. In addition, patient factors may influence the ability to perform these procedures. In patients with severe ARDS placed on extremely high ventilating pressures, performance of bronchoscopy or subglottic suctioning may not be advisable. Clinicians should select the optimal diagnostic method that is available, safe, and appropriate for the patient's clinical situation.

3.3. Costs

Bronchoscopy requires specialized equipment which in some settings may be limited in supply or may involve considerable expense. Both bronchoscopy and subglottic suction specimens need to be processed and cultures plated to identify any microorganisms.

Recommendation 4
When a clinical diagnosis of pneumonia is made prior to final isolation of pathologic organism antimicrobial sensitivities, the clinician may need to institute antibiotic therapy for pneumonia. The antibiotic chosen should be based on available information (gram stain), burn unit microbiogram (if available), and previous cultures.

4. Considerations in formulating Recommendation 4

Definitive identification of microbiologic antibiotic sensitivities may take 3–5 days. In the interim, timely treatment of pneumonia is essential. Gram stain is a rapid, low-cost option for organism class identification that can help narrow antibiotic treatment. Microbiograms provide trends in organisms for a particular ward and/or hospital but may not be available in all settings. Finally, it has been demonstrated that in burns the BAL specimen and wound cultures grow the same organism in half of the cases [197]. Hence, in the event that immediate gram stain is not available, previous wound and BAL cultures may assist in guiding therapy.

4.1. Balance of benefits and harms

Initiation of all antibiotic administration in burn patients should be undertaken thoughtfully, as each drug administered imparts risk for microbial resistance, development of Clostridium difficile, and other toxicities. Although scoring systems for predicting pneumonia exist, such as the clinical pulmonary infection score, they have limited utility in burns [198].

4.2. Values and preferences

The choice of antibiotic agents is affected by clinician preferences, institutional values, and drug availability. As such, the selected drug, route of administration, and duration of therapy will vary by institution and protocol. Antibiotic stewardship teams can be helpful in standardizing practices and limiting antibiotic use in institutions.

4.3. Costs

Timely administration of the proper antibiotic in pneumonia treatment reduces morbidity and mortality as well as overall hospital costs. However, maintenance of an up-to-date and accurate antibiogram incurs time, personnel, and equipment costs.

Recommendation 5

The duration of antimicrobial therapy for burn patients with pneumonia should be based on established recommendations for a given organism and location. In general, antibiotics should be administered for the shortest period of time needed to adequately treat the infection.

5. Considerations in formulating Recommendation 5

Due to their immunosuppressed status, burn patients are at high risk for development of resistant microorganisms. Antimicrobial stewardship is essential, and pneumonia should be treated with the shortest possible course that eradicates the infection. Reports in burn patients substantiate that ongoing monitoring for clinical signs of pneumonia and culture surveillance, particularly for virulent organisms, is optimal to assure eradication prior to terminating treatment [199]. The recommended treatment duration for pneumonia depends on the type of organism and the patient's severity of illness. For patients with VAP *not* due to gram-negative bacilli, a fixed course (7–8 days) of antibiotics may be optimal, as it does not increase the risk of adverse clinical outcomes and may reduce the emergence of resistant organisms compared to a 10–14 day course [200]. For patients with VAP due to nonfermenting gram-negative bacilli, a 10–14 day course of antibiotics may reduce the incidence of recurrent pneumonia compared to a 7-day course, but little study of this has been conducted in burn patients [201].

5.1. *Balance of benefits and harms*

The benefit of antimicrobial therapy must be weighed against the potential for drug complications, inadequate treatment, development of resistant organisms, and limited drug availability.

5.2. *Values and preferences*

The optimal antibiotic choice for pneumonia treatment in a burn patient depends on burn center experience, microbiograms, drug availability, and experience in drug administration. Antibiotic options can be limited in both high- and low-resource settings based on institutional guidelines and/or practices.

5.3. *Costs*

The cost of antibiotic administration can be contained by restricting administration to the shortest duration that effectively resolves the infection.

Recommendation 6

Ventilator-associated pneumonia (VAP) prevention bundles should be used in burn patients requiring mechanical ventilation.

6. Considerations in formulating Recommendation 6

VAP, which impacts approximately one third of critically ill patients, is associated with prolonged recovery, increased morbidity, and death in burn patients [202]. Burn patients frequently require intubation due to respiratory failure and/or upper airway obstruction, and these patients are at significant risk for the development of pneumonia. The use of VAP bundles in burn patients has been shown to reduce VAP incidence and mortality [200,202]. However, the ideal components of the bundle have not been defined. Parameters in many bundles include elevation of the head of the bed to 30°, daily oral care with chlorhexidine, minimizing sedation, changing the ventilator circuit only if visibly soiled or malfunctioning, stress ulcer prophylaxis, and deep venous thrombosis (DVT) prophylaxis.

6.1. *Balance of benefits and harms*

Given the adverse effects of VAP on patient outcomes, utilization of the VAP bundle has a great potential to benefit intubated burn patients by reducing the incidence of pneumonia and its associated complications. Two of the elements, namely stress ulcer prophylaxis and DVT prophylaxis, do not directly impact pneumonia incidence. Hence the benefit of these two components of the bundle should be carefully considered prior to instituting therapy. Likewise, daily sedation interruption may lead to inadvertent extubation in delirious patients. Sedation interruption should only be considered if it is safe.

6.2. *Values and preferences*

The most obvious method of preventing VAP is to avoid unnecessary intubation. Once intubated, patients may develop VAP. The use of DVT prophylaxis and stress ulcer prophylaxis may not contribute to VAP and are variably included in some bundles.

6.3. *Costs*

VAP prevention bundles can be performed with little utilization of supplies. Maintenance of the head of bed at 30° degrees is a quick and easy method requiring few resources. Chlorhexidine may not be available in all units; hence another agent may be required for oral care. Personnel require training to include a VAP bundle as part of burn unit protocols.

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Infections in burns: Part 3—Urinary tract infection

Recommendation 1

Insert catheters only for appropriate indications and leave them in place only as long as needed.

1. Considerations in formulating Recommendation 1

Urinary tract infection (UTI) is the most common hospital-acquired infection and the largest percentage of UTIs are related to indwelling urinary catheters [203,204]. Catheter use has also been associated with negative outcomes besides infection, including nonbacterial urethral inflammation, strictures, and mechanical trauma. Patients with urinary catheters should be evaluated daily on the need for the continued use of the catheter. These catheters should be immediately removed when no longer needed [205].

Appropriate indications for and duration of use of catheterization include: (1) when patients are expected to receive large-volume infusions or diuretics; monitor urinary output during initial fluid resuscitation; (2) an expected prolonged duration of surgery with need for large-volume infusions and/or the need to monitor intraoperative urinary output (catheters inserted for this reason should be removed postoperatively); (3) measurements of urinary output in critically ill patients; and (4) when selected patients with urinary incontinence need assistance in healing of open skin grafts [203]. Indwelling catheterization is inappropriate in patients who are incontinent or when catheterization is used as a means of obtaining urine for culture or other diagnostic tests when the patient can voluntarily void.

1.1. *Balance of benefits and harms*

The daily risk of developing a catheter-associated UTI (CAUTI) for all patient populations is estimated to be 3–7%. In burn patients, this proportion is likely to be higher, due to a potential lack of skin integrity and to higher levels of microbial colonization on the wound surface. One review of hospitalized patients noted that when routine reminders were issued to practitioners to review placement of catheters and remove them when not needed, the CAUTI rate was reduced by 53% [203]. Patients with large burn injuries often require extended use of catheters to monitor fluid intake and hemodynamics. Therefore, when possible, reducing the days of catheterization could decrease the incidence of UTI and provide real benefits to these patients.

1.2. *Values and preferences*

Not all health care staff may understand the importance of determining for which patients urinary catheterization is appropriate. In addition, the importance of removing catheters at the appropriate and earliest time may not be understood. Evidence suggests that this can be addressed through properly educating the medical and nursing staff and advising audits of the insertion techniques and daily requirement for continued catheterization. A program in six developing countries which addressed these issues resulted in a decrease in CAUTI rates from 5.9 to 2.6 per 1000 catheter-days (relative risk, 0.43; 95% confidence interval, CI: 0.21–1.0) [203].

1.3. *Costs*

The main cost related to improper insertion and removal of urinary catheters is associated with the expense of treating these infections and the subsequent impact this treatment may have on the development of multi-drug resistant organisms (MDRO). This turn of events may result in even more expensive treatment for additional infections that may develop and the costs of increased precautions to care for these patients.

Recommendation 2

When appropriate, consider using alternatives to indwelling urethral catheterization, such as external catheters (Texas catheters) or diaper-like methods for selected patients.

2. Considerations in formulating Recommendation 2

In both pediatric and adult patients, diapers can be used for those who are sedated or incontinent; if needed, diapers can be weighed to determine the urine volume. Some evidence suggests a benefit in using external catheters over indwelling urethral catheters in male patients who require a urinary collection device but do not need an indwelling catheter for urinary retention or bladder outlet obstruction. Statistically significant differences were not found or reported for the individual CAUTI outcomes or death [203]. No data showed differences in local complications such as skin maceration or phimosis when using external catheters

2.1. *Balance of benefits and harms*

Catheterization, the most common cause of UTI in the burn population, can be associated with secondary bloodstream infection. Morbidity related to a single episode of catheterization is not well described, but the high number of catheters used in the burn population means the cumulative burden of CAUTI may be substantial [203].

2.2. *Values and preferences*

Health care workers, including physicians and nurses, may not have a complete understanding of the importance of using noninvasive urinary monitoring, such as diapers, to reduce the risk of CAUTIs in this already very vulnerable population of patients. A urinary catheter checklist has been developed by many institutions to help guide appropriate selection [206].

2.3. *Costs*

The main cost of not using alternative methods over indwelling urethral catheterization is related to the cost of materials and complications associated with the development of infections, which is much more likely when indwelling catheters are in place. In the burn population, these costs must be balanced against the need for accurate urine output measurement. This cost can be effectively managed by removing these catheters as soon as possible and replacing them with either diapers or in appropriate males, condom catheters.

Recommendation 3

Use proper techniques for urinary catheter insertion. When placing urinary catheters, use aseptic technique, including hand hygiene and sterile equipment. Ensure that only properly trained persons who know the correct technique of aseptic catheter insertion and maintenance are given this responsibility.

3. Considerations in formulating Recommendation 3

Risk factors for developing a CAUTI are reduced when personnel inserting these catheters are trained to use aseptic technique and to monitor the duration of catheterization. Assessment of competency should be included in the program for those inserting catheters. An appropriate infrastructure with written guidelines for catheter insertion is recommended for all acute care hospitals. These guidelines should include documentation of an order for catheter placement and the date/time of insertion.

3.1. *Balance of benefits and harms*

CAUTIs resulting from improper adherence to aseptic technique affect many patients with indwelling urinary catheters. This is especially true in burn patients, when placement of these catheters may take place in emergent situations in the field or in emergency departments. Replacement of these catheters may also be problematic due to edema in the periurethral area as a result of the sometimes massive fluid resuscitation that these patients require, making catheter replacement unfeasible. Sustained efforts to ensure that appropriately trained personnel and aseptic techniques are used when catheters are inserted could provide benefits in decreasing the incidence of CAUTIs in this population.

3.2. *Values and preferences*

Education of health care personnel involved in inserting urinary catheter should include information on CAUTI prevention and procedures for employing aseptic technique during insertion. Competency should be assessed in these practices and should include hand hygiene immediately before insertion of the catheter. Aseptic technique and sterile equipment should be used for catheter insertion, including a drape; sterile gloves; sponges and a sterile antiseptic solution; and a sterile single-use packet of lubricant jelly. To minimize urethral trauma, use as small a catheter as possible consistent with proper drainage [203].

3.3. *Costs*

Costs include obtaining appropriate sterile equipment for catheter insertion and for drainage. Other costs involve the replacement when feasible of inappropriately placed catheters in burn patients who have had catheters inserted in an emergent situation, and the treatment of CAUTIs related to these situations.

Recommendation 4

Use proper techniques for urinary catheter maintenance. Maintain a closed drainage system and if breaks in aseptic technique, disconnection, or leakage occur, replace the catheter and collecting system using aseptic technique and sterile equipment. Maintain unobstructed urine flow.

4. Considerations in formulating Recommendation 4

A closed catheter drainage system, with ports in the distal catheter for needle aspiration of urine, should be used to reduce the risk of CAUTIs in patients with short-term indwelling urethral catheters [207]. Institution-specific strategies should be developed to ensure that disconnection of the catheter junction is minimized and that the drainage bag and connecting tube are always kept below the level of the bladder. Use soap and water for routine meatal cleansing in adult patients with indwelling urethral catheters. Daily meatal cleansing with povidone-iodine solution, silver sulfadiazine, polyantibiotic ointment or cream, or green soap and water is not recommended as a means to reduce the incidence of CAUTIs [207].

4.1. *Balance of benefits and harms*

Properly securing and maintaining urinary catheters after insertion prevents movement and minimizes urethral traction. Studies have shown that maintaining a sterile, continuously closed system with unobstructed urine flow will decrease the incidence of CAUTI [203]. Additionally, do not routinely change the drainage system as this has been shown to increase the risk of CAUTI. Routine meatal cleansing is the standard of care but may be impacted by burns in the perineal area, in which case topical antimicrobials used to treat the burn wound may also be used.

4.2. *Values and preferences*

Education of health care personnel responsible for caring for patients with urinary catheters should emphasize the importance of maintaining the system aseptically and only entering the system when needed and via insertion of a sterile needle or sterile Luer Lock syringe for aspiration of samples.

4.3. *Costs*

Costs, which are for the catheter equipment, have been significantly reduced since the discontinuation of routine changes of catheters and drainage system equipment.

Recommendation 5
Do not change indwelling catheters or drainage bags at routine, fixed intervals; but rather, make these changes based on clinical indications such as infection or obstruction, or when the closed system is compromised.

5. Considerations in formulating Recommendation 5

Studies have shown no benefit for reducing CAUTIs by routinely changing urinary catheters or drainage bags. Only if catheters or drainage bags become obstructed by debris should they be changed [203]. In patients with short-term indwelling urethral catheterization, data regarding the use of antimicrobial (silver alloy or antibiotic)-coated urinary catheter are insufficient to recommend the use of such catheters to reduce CAUTI [203,207].

5.1. *Balance of benefits and harms*

Studies have shown that decreasing the incidence of CAUTI will be achieved by replacing the catheter and collection system only with the occurrence of breaks in aseptic technique, obstruction of the catheter, or leakage [203]. This replacement may be necessary in patients with burn injury who require long-term catheterization.

5.2. *Values and preferences*

Education of health care personnel responsible for caring for patients with urinary catheters should include the importance of assessing the integrity of the catheter and drainage system. If any breaks occur or leakage is identified, the system should be replaced immediately.

5.3. *Costs*

Costs are related to the need for equipment change in cases of malfunction or other clinical indications.

Recommendation 6
Bladder instillations or washouts must not be used to prevent catheter-associated infections.

6. Considerations in formulating Recommendation 6

Certain practices should not be used routinely to reduce CAUTIs: in cases of obstruction in patients with long-term indwelling catheterization, do not irrigate catheters with normal saline; also, do not add antimicrobials or antiseptics to the drainage bag of catheterized patients [203,207].

6.1. *Balance of benefits and harms*

Studies have shown that continuous irrigation of catheters, either with normal saline or antimicrobials, is not an effective method to prevent CAUTI [203]. If catheters become obstructed they should be replaced.

6.2. *Values and preferences*

Education on the appropriate methods for handling catheter obstruction with a change of catheters and drainage equipment should be provided for everyone involved in the care of this equipment.

6.3. *Costs*

The main costs associated with maintaining catheters and preventing CAUTIs involves education of health care staff on appropriate care of these catheters and equipment.

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Infections in burns: Part 4—Wound infection

Glossary

Contamination is defined by the presence on burn wounds of nonproliferating bacteria that do not trigger a host response.

Colonization is defined by the presence within the burn wound surface of limited bacteria proliferation ($<10^5$bacteria/g) that does not trigger a host response and does not affect wound healing.

Local infection is defined by the presence deeper into the burn wounds of microorganisms at a concentration $>10^5$bacteria/g, which proliferate at a rate that triggers a host response. Local infection is still localized to the burn wounds and with no invasion into unburned tissues.

Invasive infection is defined by the invasion or destruction into the surrounding tissues of burn wounds, with microorganisms at a concentration $>10^5$bacteria/g, that are associated with local and systemic clinical signs. The infection is no longer contained and it may involve deep tissues, muscle, fascia or bone.

Cellulitis is defined by the presence of advancing erythema, induration, warmth, swelling and tenderness around the burn wound edges and it may be associated with signs of sepsis. Cellulitis requires topical and systemic antimicrobial care.

Infection is one of the leading causes of mortality in burn patients. Burn wounds are one of the most common sources of sepsis and bloodstream infection, with direct impact on morbidity, hospital length of stay, ventilator days, and health care cost.

Although burn wounds are initially sterile, they become contaminated within 48h [208]. In the next 5 days, the burn wound surfaces are colonized from the patient's normal skin, gastrointestinal tract and upper respiratory flora, as well as from the hospital environment and via health care workers' manual transfer.

In the first week after thermal injuries, the most common pathogens are Staphylococcal species and *Streptococcus pyogenes*. After that, due to their increased virulence and antimicrobial resistance, gram-negative bacteria such as *Pseudomonas aeruginosa*, *Enterobacter* species, *Proteus*, and *Escherichia coli* predominate. Antibiotic-resistant nosocomial pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), multidrug-resistant gram-negative rods, including *Pseudomonas aeruginosa*, *Acinetobacter* spp., and various *Enterobacteriaceae* spp. may appear. The use of broad spectrum antibiotics could lead to wound colonization with yeasts and fungi (*Candida* spp., *Aspergillus* spp., *Fusarium* spp., *Alternaria* spp., *Rhizopus* spp., and *Mucor* spp.)

Recommendation 1

The gold standard tool for the diagnosis of invasive burn wound infection is a quantitative culture of tissue and histologic proof of microbial invasion in viable nonburned skin biopsies. A tissue density of 10^5 CFU (colony forming unit)/g for pathogens establishes the diagnosis of burn wound infection.

1. Considerations in formulating Recommendation 1

Invasive infection is one of the main reasons for mortality and morbidity in patients with burn injuries [209]. Early detection of invasive burn wound infection leads to improved outcomes [210].

Teplitz et al. have shown that an increased load of *Pseudomonas* spp. in burn wounds in rats was associated with invasion of viable tissue [211,212]. A bacterial load in burn wounds higher than 10^5CFU/g is considered infection, as described by Herruzo-Cabrera et al. on porcine models [213]. Bacterial counts of more than 10^5CFU/g reduce wound healing and also graft take [214,215]. The bacterial load in burn wounds is determined by qualitative, semi-quantitative and/or quantitative methods.

The quantitative assessment requires tissue biopsy, which needs to be taken from deep sites beneath the eschar. It is considered the "gold standard" investigation because it confirms the diagnosis of invasive burn wound infection (providing a value of bacteria per unit volume measured in burned and uninjured tissue), and identifies the bacterial species, especially on unexcised eschar. Although the quantitative method is very important, it does not provide further information about the depth of the invasion [216]. Histologic demonstration of invasion of pathogens into adjacent uninjured tissue defines an invasive burn wound infection. The negative predictive value of the quantitative method is excellent.

However, studies have shown that the way the biopsy is sampled, processed and evaluated could lead to misinterpretation of the findings [217,218]. As quantitative cultures require a long processing time (up to 24 and 36h), it may not be clinically useful in the context of early diagnosis of sepsis

from an invasive burn wound infection. A variety of methods can determine the absolute bacterial count, but there is no "gold standard" technique [219,220].

Tips:

The semi-quantitative or qualitative assessment of bacterial load (see Recommendation 3 for further description of these methods) could be considered alternative methods to determine the diagnosis of invasive burn wound infection. In some resource-limited settings (RLS) the ability to identify the type and the density of microorganisms is not possible. The clinical signs of burn wound infection include early separation of the eschar, brown-black foci of discoloration, sub-eschar suppuration and ecthyma gangrenosum. Therefore, in these circumstances, an early clinical diagnosis of the invasive burn infection should lead the management.

1.1. *Balance of benefits and harms*

Whether quantitative methods are still valid in an era where improvements in wound care have dramatically reduced morbidity and mortality is an area of debate. The quantitative method is very useful for fungal and viral infection in burn patients because it is a substitute for histologic analysis [216,221]. The quantitative method is expensive and therefore not widely used worldwide, especially in RLS.

1.2. *Values and preferences*

The quantitative culture of tissue and histologic proof of microbial invasion in viable nonburned skin biopsies provide the diagnosis of invasive burn wound infection. The indication for performing quantitative cultures requires correlation with the local clinical features and early signs of sepsis. This indication has substantial value, especially for confirming an invasive fungal infection. In an era when early debridement is advocated, quantitative cultures are not performed often. If the patient is treated with topical antimicrobials rather than excised early, quantitative methods could provide the burn surgeon with information to direct a more targeted antimicrobial systemic therapy; this would also provide an indication for surgical debridement of the burn wounds.

1.3. *Costs*

Quantitative measures are more resource intensive (labor and cost) and sometimes these measures cannot reliably predict clinical outcomes [220]. Many burn centers switched to using qualitative and semi-quantitative methods when wound surveillance is required. In RLS where these methods are not a valid choice, the diagnosis of invasive burn wound infection is considered more on a clinical basis. If semi-quantitative or qualitative methods are available in RLS, this could provide information to better target systemic antimicrobial treatment.

Recommendation 2

Burn wound infections are initially treated with topical and systemic antimicrobial agents; when the clinical and/or laboratory evidence indicates invasive burn wound infections, urgent surgical excision/debridement is required.

2. Considerations in formulating Recommendation 2

Infection prevention in burn patients is critical. If infection is diagnosed in burn wounds, topical antimicrobials and systemic therapies will aim to reduce the bacterial load and suppress any further invasion into healthy tissues. Globally, practice varies widely between the use of topical antimicrobials and early excision [222,223]. Two randomized controlled studies have shown that patients with burns >15% total body surface area (TBSA) have similar wound infection rates if they had early burn wound excision or application of a antimicrobial topical agent [224,225].

The literature contains a limited amount of data regarding how well antibiotics penetrate an avascular burn eschar. Adequate early debridement of the infected burn wounds removes the infected tissue, improves the local perfusion, and reduces the risk of colonization with direct impact on outcomes [226,227]. If the diagnosis of burn wound infection was established, and early debridement is not an option (patient status, resource availability), increased frequency of antimicrobial application should be performed along with a targeted systemic antibiotic therapy. The presence of invasive burn wound infection will lead to prolonged hospital stay. To date, no standard methods guide the performance of antibiotic susceptibility testing on the isolated bacteria species from burn wounds versus use of topical antimicrobial agents. Invasive burn wound infection requires urgent debridement as it could lead to sepsis, increased morbidity, mortality and poorer outcomes [209].

Tips:

If resources allow, and there are surgical indications, early excision should be considered. The effects of early excision have proved numerous times to reduce local and systemic inflammation response and to reduce mortality. In the last 3 decades, the use of nanocrystalline structure of silver has revolutionized wound dressings and has been used frequently for burn wounds or grafted areas. Regular assessment of the burn wounds could provide clinical signs of invasive infection, and to avoid sepsis and reduce mortality, debridement/excision should be performed urgently along with the provision of systemic antimicrobial therapy.

2.1. *Balance of benefits and harms*

Certain factors could influence the decision to perform early burn wound excision. Some of these factors include patient status and comorbidities, extent and depth of the burn wounds, resources available (operating room, staffing, topical antimicrobial supplies, availability of temporary wound coverage) and the local burn management practice.

2.2. *Costs*

Management of invasive burn wound infection is expensive, requiring urgent debridement of the affected areas along with systemic antimicrobial therapy, and it prolongs hospital stay.

Recommendation 3

Infection surveillance of the burn wound is performed by obtaining swabs from the burn wound surface after the dressing and topical antimicrobial agents are removed and the burn wound surface is cleaned.

3. Considerations in formulating Recommendation 3

Since the introduction of performing early excision, qualitative and semi-quantitative cultures are adequate for infection surveillance, more convenient, and less resource intensive. Microbiology laboratories routinely use qualitative and semi-quantitative results from cultures of superficial wound samples and could differentiate between colonization and infection [228,229]. Collection methods differ, but prior to sampling, the wound surface needs to be clean of topical agents and ideally the surface from where the swab will be taken should be cleaned with an alcohol-based solution [229,230].

Studies that evaluated comparing qualitative and quantitative microbiology measurements have shown conflicting results and most of the studies were performed before the implementation of early excision. Steer et al. have shown a poor predictability of the bacterial counting between tissue biopsy and swab as the bacterial load varies with the depth of the burn wound and with the location of sampling [229]. It is important to emphasize that positive surveillance swabs do not dictate the need for systemic antimicrobials.

Tips:

Burn centers maintain certain protocols for burn wound infection surveillance. The swabs from the burn wounds could be taken at regular intervals, or when clinically indicated. Gram staining provides information about the degree of colonization of the wound but it does not provide information about the type of microorganisms and antimicrobial susceptibility. Swabs from the burn wound surface are used for inoculation by employing the four quadrants method with certain growth mediums. After incubation for 24h at 37°C, the plates are inspected for growth. The qualitative microbiology analysis identifies all potential pathogens and the susceptibility to preset antibiotics. The semi-quantitative analysis provides information about the nature of the pathogen (genus, species) but also about the predominance in the four quadrants.

3.1. *Balance of benefits and harms*

The qualitative and semi-quantitative methods are important to identify the difference between colonization and infection, and the bacterial species involved; but also for the burn wound infection surveillance in burn-specialized services. Swab surveillance should not lead to inappropriate use of systemic antimicrobials.

3.2. *Costs*

After the introduction of the concept of early excision, many burn centers switched to more convenient and less expensive practices such as using qualitative and semi-quantitative methods when wound surveillance is required.

Recommendation 4

Prophylactic antibiotics should not be administered to patients with burn injuries in the first 5-to-10 days after injury, to reduce the burn wound infection rates.

4. Considerations in formulating Recommendation 4

Several studies in the literature investigated the prophylactic use of antibiotics after burn injuries. The Cochrane review in 2013 did not show clear benefits for prophylaxis although inclusion and exclusion criteria were very strict [231]. Ramos et al. reviewed systemic antimicrobial use in burns. To reach a better understanding of the evidence available, they classified the injuries as nonsevere or severe and examined the type of antimicrobial used [232].

For nonsevere burns, most of the studies were conducted in a pediatric population (randomized controlled trials, prospective and retrospective studies) and did not show any difference when compared with the cohort that did not receive antibiotics. A randomized controlled study done in an adult population with penicillin for 5 days showed no difference in cellulitis and burn wound infection, but in the antibiotic administration group the incidence of gastrointestinal tract colonization with Candida was 18% [231,232].

In severe burns, five trials investigating the use of prophylactic antibiotics showed that an increased colonization with Pseudomonas occurred earlier than it did in the control cohort. Some trials in the literature, primarily from Japan, showed that prophylactic antibiotics, given to severe-burn patients who are ventilated, may reduce the risk of pneumonia as well as the mortality rate [232–234].

4.1. *Balance of benefits and harms*

Evidence from the literature regarding prophylactic antibiotics administered to patients with burn injuries <10% TBSA indicates that prophylaxis does not reduce the risk of invasive burn wound infections or cellulitis [233]. The use of prophylactic antibiotics in burns >10% TBSA did not decrease the risk of wound infection or cellulitis, but it did decrease the risk of pneumonia in ventilated patients [234]. Antimicrobials have their own side effects and could potentially cause harm. Use of prophylactics will lead also to increased resistance against strains in the burn centers and units, with no benefit to patients.

4.2. *Costs*

Any antibiotic usage comes with a cost and use of prophylactics will increase bacterial resistance, therefore requiring more expensive drugs to treat the invasive burn wound infection.

Recommendation 5

In large burn wounds, fungal infections are associated with greater mortality. Rapid diagnosis, aggressive wide debridement of the infected areas, and systemic antifungal agents are required. The diagnosis of burn wound infection with fungi and is most reliably

made by culture and histologic examination of the tissue biopsy and immunofluorescence testing.

5. Considerations in formulating Recommendation 5

Discriminating between colonization and infection in burn wounds is difficult as early clinical signs are not specific [235]. Colonization with Candida was identified as a high-risk factor for invasive infection. The Candida colonization index is clinically relevant as it links Candida colonization with clinical risk factors, total parenteral nutrition, and severe sepsis [236,237].

Studies have shown that patient-related risk factors for fungal wound infections are age, burns >40%TBSA, and inhalation injury [235,237]. Any stressors related to burn treatment that weaken the immune system (late debridement, prolonged antimicrobial treatment, blood transfusions, total parenteral nutrition, etc.) could create circumstances for fungal colonization and infection [235]. Suspicion of fungal burn wound infection, which is associated with a high mortality rate, requires a rapid diagnosis based on clinical features and histologic exam of a tissue sample [238]. Histologic diagnosis, though a reliable diagnostic method for fungal infection and colonization, is not used routinely due to its invasive approach [239]. Real-time polymerase chain reaction assay is an early and noninvasive method, but is not widely available due to its high cost [240]. This assay is also not available for fungal organisms. The management of fungal infection involves early treatment with antimycotic treatment and urgent excision or re-excision of the involved areas and wound closure, as it is associated with high mortality [241,242]. In cases of Aspergillus, frequent surgical exploration is required to avoid limb amputation.

Important note: In the burn population, early clinical signs of colonization with Candida increase the risk for developing invasive infection with a high mortality.

Tips:

Although direct confirmation of positive cultures for fungi is the standard diagnostic approach, it is not fast (there is a latency period) and the species identification process is not reliable. To reduce the risk of colonization and infection with yeast, avoid allowing a moist environment on burn wounds and prolonged antimicrobial treatment; these suppress bacterial flora and increase the potential for colonization with Candida albicans. Candida species are the most frequent yeast grown in burn centers [236].

5.1. *Balance of benefits and harms*

Prompt diagnosis of fungal infection is essential and quantitative tissue biopsy could support the clinical diagnosis. Fungal infections are difficult to treat and debridement of the affected wounds should be performed as early as possible.

Recommendation 6

Diligent compliance with infection control practices (physical isolation in a private room, use of gowns and gloves during patient contact, and hand washing before and after each patient visit) and the use of a laminar airflow isolation room reduces the risk of burn wound infection with nosocomial bacteria.

6. Considerations in formulating Recommendation 6

The risk of infection from exposure to bacteria is higher in burn patients than for almost any other hospital patients. Contact precautions and hand hygiene are mandatory and standards need to be followed closely [243]. Once the patient is admitted to a burn-specialized service, infection control practices should be implemented to minimize the risk of infection on these patients who have a suppressed immune system associated with the burn pathophysiology [244,245]. To minimize the risk and reduce the incidence of infections with antibiotic resistant organisms, routine hand hygiene before and after contact with any patient is mandatory [208]. Cross contamination is reduced by using isolation rooms and laminar flow [246]. Immersion hydrotherapy treatment (Hubbard tanks) was considered one of the main culprits for nosocomial transmission of microorganisms (*Pseudomonas* spp.) to burn wounds until the 1990s [247,248]. Showering provides a better environment for the cleaning and debridement of the burn wound and reduces the transfer of microorganisms, but outbreaks of MRSA were documented in the literature [249].

6.1. *Balance of benefits and harms*

Compliance with strict infection control practices is required to reduce the incidence of outbreaks with virulent bacterial species and to reduce the cross contamination of burn patients in intensive care units and in burn centers.

6.2. *Costs*

Diligent compliance with infection control practice is cost-effective as it will reduce the cost of and resources required for treating the burn wound infection.

Recommendation 7

Burn centers should routinely monitor the microbial profile of burn wound colonization, the antimicrobial susceptibility profiles of microorganisms implicated in burn wound infections, and trends in the nosocomial spread of these pathogens.

7. Considerations in formulating Recommendation 7

Infection control plays an essential role in any burn center's prevention program. Burn wound infections should be rigorously monitored to create an accurate epidemiologic profile about infection rates and to avoid antimicrobial resistance trends, as infection represents a serious challenge for burn surgeons [208,250–252]. Routine surveillance should take place for other burn-related types of nosocomial infections such as catheter-related infections, pneumonia, and urinary tract infections. Culture surveillance (e.g., culture

of nasal, rectal, or groin swabs for MRSA and culture of rectal swabs for VRE) as well as routine microbial surveillance cultures of burn wounds, blood and urine allows burn-specialized services to identify epidemic pathogens and any antibiotic-resistant strains [250,251]. A strict policy should be instituted in burn centers regarding appropriate antimicrobial selection for the treatment of infection in burn patients. In this way, the burden caused by antibiotic resistant organism-related illness could be avoided and hospital cost and length of stay could potentially be reduced. Antibiotic utilization should be rotated or changed based on each burn center's process for ongoing monitoring of antibiotic resistance [253].

Tips:

Some burn centers conduct regular surveys of the burn wounds on patients. The results help target the selection of appropriate systemic antimicrobial agents when a treatment needs to be started empirically [254,255]. The antimicrobial susceptibility profiles will vary due to the variety of microbial flora in each burn center. This will have direct implications on the choice of an adequate antimicrobial for empirical treatment decisions, both for early invasive wound infection or for sepsis derived from other sources [251,256].

7.1. *Balance of benefits and harms*

A lack of culture surveillance and of monitoring the bacteriologic profile in burn-specialized services could lead to frequent outbreaks of antibiotic-resistant bacteria and fungal infections via nosocomial spread, with direct impact on health care cost, mortality and morbidity.

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Management of indwelling catheters

Preamble: The complexities of modern burn care often necessitate the immediate and prolonged use of vascular access devices (VADs), including central venous catheters (CVCs), peripherally inserted central catheters (PICCs), midlines, arterial lines and peripheral intravenous (PIV) cannulas. These devices play an important role in diagnostic and therapeutic care, such as fluid replacement, resuscitation, and hemodynamic monitoring, as well as medication and nutrition delivery. As such, they are a cornerstone of quality burn care; however, because of their invasive nature, they come with substantial risks of both infective and mechanical complications. Vascular access devices are potential sources of bloodstream infection (BSI); central line-associated bloodstream infection (CLABSI) in particular, is associated with significant morbidity and mortality in the severely ill [257–259], while CLABSI and other catheter-related BSI are independent predictors of increased health care expenditure and hospital length of stay (LOS) [260–262]. For patients with severe burn injuries, risks of infectious complications are increased by the cumulative effects of burn wound colonization, systemic immunologic changes, and the need for long-term vascular access.

These guidelines set out best-practice recommendations for the selection, insertion, and management of VADs in patients with burn injury. Other VADs such as tunneled, cuffed CVCs, long-term hemodialysis catheters and implanted ports are not a focus of this guideline as they are rarely used in the acute setting and are discussed in detail in other texts [263,264].

Recommendation 1

Select the most appropriate vascular access device for the intended use. Factors to consider include therapeutic needs, monitoring requirements, and the characteristics of each vascular access device.

1. Considerations in formulating Recommendation 1

Careful consideration must be given to selecting the most appropriate device that meets the patient's therapeutic requirements, while also posing the lowest risk of infective

and mechanical complications. No one device is suitable for all scenarios and the choice of VAD is affected by the patient's premorbid state and severity of burn injury. Decisions are complex, and although guidance tools, such as the Michigan Appropriateness Guide for Intravenous Catheters [265] (MAGIC) and the Vessel Health and Preservation (VHP) pathway [266] are available, none have been specifically validated in a burn-injured cohort. Considerations include:

Therapeutic needs:

Therapeutic infusion requirements should guide safe and appropriate VAD choice. Multiple concurrent infusions may be essential in critically ill patients but the desire for extra lumens must be balanced against the rising risk of thrombosis with increased catheter diameter. Consideration of the locally toxic or vesicant effects of some agents used commonly in burn care such as inotropes, some antibiotics and less commonly parenteral nutrition, make them unsafe for peripheral infusion, and as such, often necessitate a central venous device. Reference lists of agents unsuitable for peripheral administration are available [267]. It is also important to consider the expected duration of infusion requirements, as different devices have inherent advantages or disadvantages, depending on whether short- or long-term therapy is required [268]. Needs for hemodynamic monitoring should also be considered. Arterial lines are the only choice for invasive blood pressure monitoring and repeated access for blood gas analysis, whereas CVCs are the only choice for central venous pressure monitoring requirements.

Characteristics of vascular access devices:

The different characteristics of VADs need to be considered when making good device choices. In each situation, clinicians need to consider the catheters' discrete design advantages, which meet different therapeutic requirements, while also weighing the different risks they pose. VADs are the single most important cause of health care-associated BSI, with disparate risks associated with different devices. A systematic review analyzing 200 VAD studies found BSI rates from nontunneled CVCs were 2.7 per 1000 VAD days; inpatient PICCS 2.1 per 1000 VAD days; arterial catheters 1.7 per 1000 VAD days; and peripheral vascular catheters 0.1 per 1000 VAD days [261]. While the lowest risk of BSI was associated with PIVs, these findings are confounded by the heterogeneity of patient populations, and the illness severity of patients requiring each type of VAD.

Use of peripheral intravenous catheters is one of the most commonly performed hospital invasive procedures [269]. These catheters establish short-term intravenous access into the smaller veins of the upper extremities, and less frequently the lower extremities. They are useful in the treatment of patients with smaller, and/or uncomplicated burn injuries, who usually only require short-term vascular access. However, despite their ubiquity in health care they have limitations and pose a challenge to insert, with each repeat attempt creating a portal for microorganism entry. A recent systematic scoping review on insertion tools identified that prolonged and repeated insertion attempts can lead to classifying the patient with the label of difficult intravenous access (DIVA). The review suggests better clinical assessment tools are needed to improve insertion outcomes [270].

Given the clinical reality that burn patients' first VAD is likely to be a PIV and that these patients may present with fewer venous and arterial options, a pragmatic approach underpinned by evidence in this select population is needed. Despite the lack of evidence of specific clinical processes for vascular access in burns, emerging evidence suggests DIVA patients require a team approach to reduce failed attempts and increase first-attempt success. One study improved first-time insertion success with ultrasound guided PIV insertion in 9 out of 10 patients and their pain scores were also reduced. While this approach could be considered, it is resource dependent [271]. Additionally, PIVs are inappropriate for some medications [267], cannot be used for hemodynamic monitoring, are no solution for long-term access requirements, and in burn populations, the burn characteristics can limit access to preferred peripheral sites. The size of PIV has been demonstrated to influence PIV survival rates in adult cohort studies, with an increased risk of thrombosis from large-diameter PIVs and an increased risk of dislodgement and occlusion with small-diameter PIVs [272,273]. As such, 20G PIVs have been recommended in adult populations [273,274]. A large cohort study involving 40,620 PIVCs in 38,161 patients from 406 hospitals in 51 countries demonstrated international compliance rates of 67% for adult PIV size recommendations [275].

Risks and costs associated with PIV-related BSI should not be underestimated. A systematic review found the incidence of PIV-related BSIs was 0.18% among 85,063 PIVs, and risk factors that were identified for PIV-related BSI were cited as prolonged PIV dwell time and insertion under time-critical conditions [276]. In the context of the millions of PIVs inserted worldwide, they create significant morbidity and additional health care costs [277–279]. Burn centers need evidence-based strategies and protocols for the routine monitoring of PIV sites, early detection and management of PIV-related BSI, and the removal/replacement of catheters. The utility of PIVs can be increased by the use of imaging techniques including ultrasound and near-infrared spectroscopy to complete a pre-insertion assessment that includes nonvisible or nonpalpable veins. Such techniques, ultrasound in particular, can be used to assess the vein structure, by measuring the diameter of the target vein, and to identify and avoid valves within a vein. The pre-insertion assessment can maximize first-attempt success but also reduce PIV failure and thus prolong dwell time and minimize the need for recurrent insertions.

Central venous catheters are used frequently in burn care, particularly in patients with severe or complex burn injuries. A CVC is usually inserted in the axillary/subclavian or internal jugular vein with the catheter tip positioned in the lower third of the superior vena cava or in the right atrium. Central access can also be achieved via the femoral vein. CVCs provide short-term critical access for up to 14 days, and can have single or multiple lumens with the option of antimicrobial coating/impregnation. There are increased risks of BSI associated with multilumen CVCs [280], which are required frequently in patients with severe burn injuries. Cuffed devices for tunneled insertion provide long-term access with a lower risk of BSI but are rarely appropriate in the acute setting. These recommendations give particular attention to noncuffed CVCs because of their frequent use in burn care, and also their significant risks.

Peripherally inserted central catheters are inserted via a peripheral vein in the upper arm, again with the tip positioned around the cavoatrial junction, and are used frequently for long-term access in burn care [281]. They have some similar characteristics to CVCs, coming in various sizes with single or multiple lumens, and can also meet many of the same therapeutic requirements. PICCs provide central venous access for up to 3 months or even longer, which in the right situation has distinct advantages over CVCs when the duration of therapy will be protracted. A notable complication particularly associated with PICCs is upper limb venous thrombosis, which complicates around 2% of PICCs in the general hospital population [282]. A systematic review demonstrated no difference in infection rates between CVCs and PICCs but higher mechanical complication rates such as catheter dysfunction and thrombophlebitis associated with PICCs [283]. Current evidence regarding PICC use in burn care indicates they have comparable safety profiles to CVCs, and should be used according to clinical judgment. A retrospective review of PICC use in 104 burn patients found that 16% of cases experienced complications [284]; the majority of these cases were superficial phlebitis with one infection and no cases of deep venous thrombosis (DVT). The authors of another retrospective single-center study comparing the safety of PICCs to CVCs in burn patients concluded that they both have similar complication rates and are associated with significant and potentially fatal risks [285]. A further retrospective study comparing complications of PICCs to CVCs found that CLABSI rates were higher for CVCs, with 6.6 CLABSI per 1000 CVC catheter days, compared to 0 per 1000 PICC catheter days. No thrombotic complications developed due to CVCs; there was one right upper extremity DVT associated with a PICC, and neither group had any technical complications [286]. Another study found that percent total burn surface area (TBSA) burns, LOS, and time from admission of PICC insertion were independent predictors of PICC-related infections [287].

Midline catheters are shorter (10–20 cm) devices that are also inserted in the veins of the upper arm. They can provide medium-term vascular access for up to 4 weeks but should only be used for medications that are suitable for peripheral administration.

Arterial catheters are used for hemodynamic monitoring and repeated blood sampling in patients with severe burn injury. Studies in non-burn populations indicate that rates of colonization and infective complications were similar between arterial catheters and CVCs [288], and rates of severe mechanical complications were low [289].

1.1. *Balance of benefits and harms*

Clinicians must consider the different characteristics of VADs in the context and complexity of each burn patient's clinical presentation and therapeutic needs, to select the most appropriate device which also poses the smallest additional risk to the patient. Any single device may not meet all requirements. In each situation, clinicians need to consider the discrete design advantages that meet different therapeutic requirements while also weighing the different risks they pose.

1.2. *Values and preferences*

Knowledge of the characteristics of different VADs and how they work, along with their limitations and risks, can help support clinical decision-making. In the right conditions, PIVs are the device of choice for their relatively low risk of BSI compared to other VADs [261], as well as their distinct advantages in providing relatively uncomplicated vascular access. In the immediacy of emergency department resuscitations of patients with severe burn injuries where time-critical interventions rely on the success and timeliness of VAD insertion, CVCs are often preferred, as the use of anatomic landmarks to guide insertion is comparatively faster than the ultrasound guidance required for PICCs, and this expedites the insertion process. However, as will be discussed, some studies suggest ultrasound guidance expedites treatment commencement because it can bypass the requirement for radiologic confirmation of catheter position.

1.3. *Costs*

VAD costs should be considered in broader terms than just that of financial expenditures. Patients and health care organizations bear the costs of VAD complications and failures. Estimated catheter-related BSI costs within the intensive care unit (ICU) adult population are significant [290,291], and are associated with higher mortality [292]. Due to widespread use, risks of PIV-related BSI are not insignificant, nor are their costs, and failure rates are high [293] which can cause treatment delays, unnecessary exposure to repeated insertion risks, pain, and increased human and financial resources. Clinicians should be judicious in making VAD choices to ensure quality, safe and cost-effective care.

Recommendation 2

For the site of catheter placement, consider patient characteristics and clinical scenario. Other considerations follow.

- ***All indwelling vascular catheters should be placed through unburned skin where possible, preferably far from the wound, to prevent contamination of the insertion site.***
- ***The forearm is the preferred insertion site for peripheral intravenous cannulas.***
- ***For central venous catheter placement in adults, the axillary/subclavian site is preferred over the internal jugular and femoral routes.***
- ***The preferred site for arterial line placement is the radial artery if available.***
- ***An upper extremity is the preferred site for peripherally inserted central catheter insertion.***
- ***Where available, ultrasonography should be used to guide catheter insertion, particularly for arterial lines in pediatric patients.***

2. Considerations in formulating Recommendation 2

Various anatomic sites can be considered for insertion of VADs, each with different inherent therapeutic advantages as

well as infective and mechanical risks. Recommendation 2 comprises a subset of recommendations related to the site of VAD insertion.

Patient characteristics and clinical scenario

When selecting the site of catheter placement, the condition of both the skin entry point and target vein must be considered. A skin entry point providing an adequate platform for dressings should be selected, avoiding hair-bearing areas, skin creases, and old scars as well as acute burn wounds, as discussed below. In obese patients, peripheral veins are often neither visible nor palpable, the basilic and brachial veins favored for PICC insertion may be reduced in caliber or too deep to access safely, and the landmarks used to guide CVC placement may be obscured. Prior vein trauma from illicit intravenous drug use, previous devices, phlebotomy or attempted access as well as complications including stenosis and thrombosis can make venous access difficult.

Where possible, place all indwelling vascular catheters through unburned skin

Vascular access devices ideally should be placed through non-burned skin, at least 5cm away and preferably far from the wounds to enable effective insertion-site management and reduce infective complications. In some circumstances, however, in the absence of alternative access sites due to factors including size and location of the burn injury, insertion through burned tissue is necessary, and is a routine burn-center practice [281]. Insufficient evidence supports being able to accurately assess the benefits and harms of VAD insertion through burn-injured skin when access options are limited; evidence is also insufficient on available risk-reduction strategies in the setting of contemporary surgical burn care and with current vascular access techniques, devices and dressings. The risk and rate of colonization of the insertion site is consistently shown to be higher in burned than in uninjured skin and this is likely to correlate with increased risk of BSI [294,295]. However, as highlighted elsewhere [296], the comparative risk associated with VAD insertion through skin in its various states after injury (undebrided, open, granulating, allografted, autografted or scarred) has not been systematically investigated and warrants a large, prospective, multicenter study incorporating modern practices including the use of antimicrobial-impregnated catheters and dressings. As advanced ultrasound-guided techniques become more widely adopted, subcutaneous tunneling of catheters from an insertion site through intact skin to a target vessel underneath burned skin should also be explored. Insertion of VADs through burned skin remains a necessary procedure and will always carry a higher risk; pragmatically, all available measures to reduce the chance of BSI should be employed, and prioritization of early debridement and grafting of the neck and upper chest should be considered to provide a safer area for VAD placement.

The forearm is the preferred insertion site for PIVs

The forearm has been recommended as the site to use for PIV insertion because of the benefits afforded by the flat surface area for dressing securement, and lack of flexion areas, which increases PIV longevity and decreases risks of mechanical failures [272,297]. We found no evidence in the burn literature related to PIV use. It has been demonstrated in a large multisite cohort study that general compliance with forearm PIV insertion recommendations is poor [275]. Burn centers need to implement protocols and strategies that increase compliance with forearm PIV insertion recommendations, while also allowing for exceptions when other factors such as burn location make this practice prohibitive.

The axillary/subclavian site is the preferred insertion site for CVC placement in adults

The optimal site of insertion for CVCs in burn patients remains controversial. In adults, an axillary/subclavian site should be used in preference to an internal jugular or femoral site. This recommendation is based on a meta-analysis that showed that axillary/subclavian sites may be associated with lower risk of catheter-related BSI than femoral or internal jugular insertion sites [298]. It is further supported by a more recent large randomized, multicenter trial showing that axillary/subclavian sites had lower rates of BSI (and DVT) than jugular or femoral sites, although there was a higher risk of pneumothorax [299]. Consequences of CLABSI complications are significant [300], and their risks increase over time secondary to length of time the catheter is in situ [261]. Considering these factors in the context of the need for long-term vascular access in immunocompromised patients with large burn injuries, a basic recommendation for the axillary/subclavian site was supported.

Consequences of mechanical complications such as pneumothorax and arterial puncture are inarguably significant [301]. However, as complications of insertion technique, these risks are immediate but short-lived, and can be minimized with the use of ultrasonographic guidance [302,303]. Risks of infective complications, on the other hand, are immediate and long-term, increasing over time, and are of great significance to the immunocompromised severely burned patient; as such, we believe the benefits of lower risks of infection with axillary/subclavian sites outweigh the higher risk of mechanical complications.

Location and proximity of the burn as well as any concurrent injuries may affect the risks associated with some CVC access sites. Furthermore, given the limited burn-specific evidence regarding the choice of CVC insertion site, while we recommend the axillary/subclavian site for CVC insertion, we recognize and recommend that decisions be made on a case-by-case basis with consideration given to the presentation of the burn injury, and availability of access sites. In some circumstances, use of the internal jugular or femoral site maybe the best choice given the complexity and variability of the other considerations, which we have attempted to describe in these guidelines. The tip position of upper-body CVCs should be confirmed by chest x-ray, fluoroscopy, and ultrasound or intracavitary electrocardiogram prior to use.

An upper extremity is the preferred site for peripherally inserted central catheter insertion

Current limited evidence indicates that PICCs have comparable safety profiles to CVCs in burn and other patient cohorts [283,284]. An upper extremity is the optimal site for insertion in adults and, when accessible, the right arm should be used in preference to the left as it has been associated with less frequent complications [304], probably even in left hand-dominant patients [305]. For pediatrics, either upper or lower extremity, or scalp veins can be used [260]. In all ages, a reduction in the risk of venous thrombosis can be achieved by

selecting the largest caliber vein and the smallest diameter catheter to maximize with catheter/vein ratio [306,307].

The preferred site for arterial line placement is the radial artery

Current evidence does not give clear guidance on the best approach to the selection of arterial catheter site in burn patients. Expert opinion within the burn and wider health care community supports a preference for the radial artery, with the femoral site as a suitable alternative. We found little evidence relating to the management of arterial lines in the burn-specific literature. One observational study reporting on 81 pediatric patients concluded that the femoral artery can be associated with a low rate of mechanical and infectious complications in children who require prolonged arterial access [308]. A 2014 systematic review drawing on a broader evidence base found that femoral insertion was associated with a greater infection risk [309]. However, that finding was challenged on the reasonable grounds that the most recent studies included in the meta-analysis did not show a difference [310]. The Centers for Disease Control (CDC) recommend the use of the radial, brachial or dorsalis pedis sites for arterial catheter insertion over the femoral or axillary sites in adults [260]. The CDC also recommends the radial, dorsalis pedis and posterior tibial in children and avoiding the brachial site. In regard to mechanical complications, a retrospective observational study compared accidental catheter removal (ACR) of arterial catheters to that of femoral and radial artery sites. ACR rate was lower for femoral arterial access than radial, and was also statistically significant when considered by '100 catheter days' [311]. Additionally, the authors of a 2002 systematic review on complications of peripheral arterial catheters found that rates of major complications were similar for radial, femoral and axillary arteries, and that the best catheterization site should be selected individually for each patient as each location has advantages and risks [312]. In the context of these studies, we recommend the radial artery as the preferred site of arterial line placement.

Where available, ultrasonography should be used to guide catheter insertion

This recommendation is based on evidence from several studies that demonstrate the significant benefits of ultrasound guidance in improving VAD insertion success rates, and reducing mechanical complications.

The use of ultrasound for the insertion of CVCs in both adult and pediatric populations has been demonstrated to improve success rates when compared to the use of digitally palpating anatomic landmarks [313]. In adult populations, using ultrasound has also resulted in significantly fewer mechanical complications and reduced procedural times [314]. While many studies focused on the internal jugular vein CVC insertion [313], benefits of ultrasound guidance were also identified for both axillary/subclavian [315] and femoral CVC insertion [316].

Furthermore, there is strong evidence to support the use of ultrasound to guide arterial catheter placement in the radial artery [317–319], as well as some evidence of the benefits for difficult PIV insertions [320]. Evidence-based ultrasound-guided VAD recommendations are available [321]. While ultrasound guidance is not routinely used for the insertion of VADs in burn care currently [281], modern approaches to vascular access during assessment, insertion and post insertion use ultrasound technology, and burn centers should ensure that clinicians are skilled in the use of ultrasound for VAD procedures.

2.1. *Balance of benefits and harms*

These recommendations for preferred VAD insertion sites presume the ideal clinical scenario, which is often not the case. Multiple factors that are discussed in these guidelines may affect the availability of and risks associated with some access sites. Clinicians should exercise good judgment when making decisions regarding choice of insertion site to ensure that choices are made with consideration toward the risks associated with different insertion sites in the context of the heterogeneity of each case.

As discussed, in patients with large burn injuries, access to VAD insertion sites is often limited and insertion through or near the burn wound is often necessary. Strategies including the use of antimicrobial-impregnated catheters, antimicrobial dressings and creams, early excision and wound closure of the area, and catheter rotation as soon as possible should be implemented to help mitigate the risks of BSI.

2.2. *Values and preferences*

Patients with a history of difficult venous access as well as those with predicted difficult access should be identified early to avoid multiple failed insertion attempts which are associated with vein trauma and other complications. Such patients should be referred to experienced operators to identify the most appropriate VAD, site, and insertion technique to establish safe and reliable vascular access. Furthermore, during the recovery phase following burn injury, VADs that have the least impact on patients' physical therapy will allow for improved short- and long-term functional outcomes.

2.3. *Costs*

Health care costs associated with site insertion are related to the ongoing training requirements of clinicians to ensure adequate skills and knowledge regarding safe practice. While conjecture remains regarding the cost-effectiveness of using ultrasound guidance routinely for VAD insertion [322], ultrasound has clearly established its clinical benefits in terms of insertion success rates and significant reductions in mechanical complications.

Recommendation 3

Clinicians inserting VADs should be trained and credentialed accordingly.

3. Considerations in formulating Recommendation 3

Clinicians should only insert VADs once they have been trained and are recognized to be competent to do so. This involves specific training and credentialing for each type of device. This recommendation is based on outcomes from

several studies in the broader literature that demonstrate the benefits of investment in adequate training and credentialing for clinicians to insert CVCs with the aim of reducing the risks of BSIs and other complications [323,324].

The CDC recommends training clinicians regarding the insertion and management of VADs, and it advocates for continuous training to maintain credentialing [260]. The Society for Healthcare Epidemiology of America (SHEA), and the Infectious Diseases Society of America (IDSA) Practice Recommendations for the Prevention of CLABSI in acute care hospitals also propose that hospitals should ensure appropriate education of staff [325]. Studies of the effects of clinician training and credentialing in reducing VAD-insertion complications in burn populations are required.

3.1. *Balance of benefits and harms*

Over 30 years ago it was identified that the health care worker providing insertion and/or care and maintenance was responsible for VAD complications [326]. As a result, specific training, credentialing and validation were recommended. Such initiatives have been demonstrated to reduce the risks of infective and mechanical complications associated with VAD insertions [323]. Vascular access teams can provide a point-of-care approach and should be incorporated into the multidisciplinary burn team where available; these teams are associated with greater insertion success and reduced insertion complications [327]. However, this approach may be seen as deskilling burn clinicians in training because procedural exposure is minimized.

In terms of clinical training and proctoring, what is recommended to establish competency is the quality of insertions measured by a set of globally accepted standards as opposed to procedural quantity [323]. However, few interventional studies have identified the causal impact of any education on vascular access procedures [328]. To maximize the benefits within the burn-injured cohort, dedicated simulation in vascular access using burn scenarios as well as reflecting on real cases could guide the development of burn-specific care and maintenance bundles to target specific risks for catheter-related BSI. It is suggested that hospital policies for VAD insertion recognize exposure to training and simulation that clinicians receive at either scientific meetings, or within particular training schemes, to be sufficient.

3.2. *Values and preferences*

Limited evidence addresses the ideal education and training requirements for the insertion and maintenance of VADs, and practices vary. Credentialing should involve an annual combination of education and supervised practice, and increasing evidence recognizes the benefits of simulation training in improving the efficiency and safety of VAD insertion and maintenance practices [329,330]. To better ensure safe and quality care, consensus guidelines are available in the literature to guide health care organizations in establishing and standardizing educational courses that also measure competency [323].

Nursing education programs should place a strong emphasis on safe PIV insertion given that internationally, nurses are the predominant group inserting PIVs [275]. Infusion or vascular access specialist teams with advanced VAD knowledge and skills are used in some clinical settings. A Cochrane review failed to find any randomized controlled trials to determine their effectiveness [327], however the Infusion Nurses Society endorses the roles of specialist teams within health care organizations because of high rates of VAD- and infusion-related complications [331]. Ultimately, the availability of specialist VAD teams to support burn clinicians in providing quality care is dependent on the wider organization in which the burn center is located.

3.3. *Costs*

Various observational studies have demonstrated the benefits of VAD education and training programs in reducing BSI rates and associated health care costs [332,333], though their significance varied [334]. Well-implemented educational programs that include strategies reinforcing desired behaviors are even more likely to improve the quality of care.

Recommendation 4

CVC care bundles should be used to reduce the incidence of bloodstream infections.

4. Considerations in formulating Recommendation 4

The benefits of CVC insertion bundles are well documented [335–340]. First developed by the Institute for Healthcare Improvement, CVC insertion bundles are designed to provide a more consistent approach to the applications of evidence-based practices that are known to reduce risks of BSIs. Central-line insertion bundles generally include a small set of evidence-based practices that apply to most situations, such as the following.

- *Hand hygiene*: use of either a waterless, alcohol-based product or antibacterial soap and water with adequate rinsing contribute significantly to the reduction in cross infection in health care environments [260,325,341,342]. This is an integral central line bundle component to reduce risks of device contamination and should be completed before and after catheter insertion, replacement, or removal, as well as when accessing the device or the dressing.
- *Maximal barrier precautions*: gown, gloves, mask and cap should be worn by the clinician to reduce immediate device colonization during CVC insertion [260,343].
- *Skin preparation*: A 70% isopropyl alcohol-based preparation with at least a 0.5% chlorhexidine gluconate component should be used for decontamination of the insertion site [260,325] and the site should be allowed to dry prior to device insertion as a means of reducing the risk of device colonization [260,344].
- *Removal*: CVCs should be removed promptly when they are no longer required because the risk of infective complications increases with duration of use [260,325,345].

Beyond insertion, bundles are also increasingly being used for the maintenance of CVCs. A recent systematic review and

meta-analysis showed a statistically significant reduction in the incidence of CLABSI after implementation of both maintenance and insertion bundles [335]. Similarly, bundles with similar evidence-based strategies have increasingly been used in the management of other types of VADs including PIVs and PICCs, though the evidence of their efficacy is not strong [346,347]. Also, in a single-center burn patient cohort, before and after the study, a multimodal CVC bundle contributed to achieving and sustaining zero CLABSI rates [348]. Further research regarding the benefits of bundle approaches in the insertion and management of other VADs, as well as in burn and other patient populations, is necessary.

4.1. *Balance of benefits and harms*

The changes that care bundle practices create to the process and communication of clinical care, in the form of checklists, and changes to processes in multidisciplinary team rounds, are often responsible for the success of reducing CVC BSI complications [345]. Importantly, burn centers should ensure strategies for good implementation and high compliance of VAD bundles as BSI and CLABSI rates are unlikely to decrease otherwise [349]. Overall, given the benefits of bundles for insertion and maintenance of CVCs, we recommend their use for CVC management and where practicable for other VADs.

4.2. *Values and preferences*

CVC bundles are often custom designed for specific patient populations and environments. Bundles often include other elements such as preferences for insertion site, kits containing all the equipment needed for catheter insertion, and educational clinical leadership and infection risk programs, which have been addressed elsewhere in these guidelines. Bundle customization has allowed health care organizations and/or teams to systematically address identified gaps in local processes [336,337]. Burn centers should also consider implementing CVC bundles that meet their local context requirements and include intermittent review of content based on findings of continuous surveillance programs.

4.3. *Costs*

Several studies demonstrate the cost benefits of using bundles in reducing CLABSI and reducing costs associated with additional measures such as using antimicrobial-impregnated catheters, whose benefits are less significant when the bundle is performed correctly [350,351]. Bundle consumables are generally inexpensive; however, costs required for monitoring and educational activities are not insignificant. It is possible that implementation of CVC bundles will not result in immediate health care savings; however, health care organizations must be prepared to invest resources into CVC bundles as well as other infection control measures, to see the reductions in both BSI rates and associated costs which lead to improvements in patient outcomes and efficiency.

Recommendation 5
Antimicrobial-impregnated/coated catheters should be used where available.

5. Considerations in formulating Recommendation 5

Use of antimicrobial-impregnated CVCs is increasing in burn care. Limited retrospective observational studies in burn populations compared the use of antimicrobial-impregnated CVCs and PICCs to their standard counterparts, and demonstrated their efficacy in reducing CLABSI rates [352,353]. The evidence supporting their use in non-burn populations is stronger, including the 2016 Cochrane systematic review showing that antimicrobial CVCs reduce CLABSI rates and catheter colonization in ICU settings [354], and a randomized control trial in a pediatric cohort [355]. Furthermore, one systematic review suggested that antimicrobial PICCs can also reduce CLABSI rates in other high-risk groups [356].

5.1. *Balance of benefits and harms*

The benefits of using antimicrobial-impregnated CVCs to reduce catheter-related BSI in severely ill populations have been demonstrated with high-quality evidence. Questions regarding the effectiveness of antimicrobial-impregnated lines relate more to their relative benefits in low BSI-risk patient populations [354]. Various antimicrobials have been used to coat or impregnate catheters including silver compounds, chlorhexidine and a variety of antibiotics. Any of these agents have the potential to cause hypersensitivity; chlorhexidine in particular has been associated with anaphylaxis, however the reported incidence remains very low [357]. Although antibiotic resistance remains a concern with more widespread implementation, this has not been observed in the trial setting [358].
A common criticism of these studies, as well as that of studies of antimicrobial-impregnated dressings, is that the benefits of these interventions appear greater when the baseline infection rate is high. When infection rates are approaching zero due to excellent standards of care, the minimal incremental gain is possibly outweighed by potential harm from the addition of antimicrobials. However, given that the baseline risk of BSI is elevated in the major burn population, the additional benefits of antimicrobials are usually clinically relevant.

5.2. *Values and preferences*

Availability of antimicrobial-impregnated catheters may be restricted in resource-limited settings (RLS). In these circumstances where possible, an increased emphasis should be placed on other risk-mitigating strategies, described elsewhere in these guidelines, to reduce the odds of BSI.

5.3. *Costs*

Antimicrobial-impregnated VADs are more expensive than standard VADs, however studies have demonstrated the cost benefits of using antimicrobial-impregnated catheters to reduce CLABSI in ICU populations [359]. Health care policies should balance antimicrobial impregnated-VAD cost outlays against the cost savings from avoided bed days from the

absence of BSI, particularly for high-risk groups including patients with severe burns.

Recommendation 6

Local guidelines for the ongoing management of indwelling vascular catheters should address: dressing choice; daily assessment of the site and monitoring of complications; accessing VADs; and catheter replacement/rotation.

6. Considerations in formulating Recommendation 6

Recommendation 6 consists of a subset of recommendations regarding the ongoing management of VADs. While there is evidence of the benefits of staff awareness and continuous follow-up of ongoing care in reducing BSI in the broader literature [335], there is limited evidence or consensus regarding the ongoing maintenance of VADs in burn patients, and wide variations in practice exist [281]. Many of the evidence-based practices described previously in Recommendation 4 regarding the use of CVC insertion care bundles are equally relevant for the ongoing management of VADs. These practices include hand hygiene, antisepsis at the entry site which can be extended to use of injection hubs, ports and the dressings, as well as the regular review of the ongoing need for the VAD.

Dressings

VAD dressings serve the dual purposes of protecting insertion sites from microbial contamination and securing the VAD to avoid dislodgement or accident removal. Dressings should be applied using sterile technique, and for areas where the underlying skin is intact, a chlorhexidine-ethanol solution should be used to disinfect the area and be left to dry [260]. It is inappropriate to use alcohol/chlorhexidine gluconate-based products when the VAD needs to go through burned tissue due to increased risk of pain and irritation. In these circumstances, povidone-iodine swabs can be used [360].

When available, antimicrobial-impregnated dressings should be used to cover CVC insertion sites. This recommendation is founded on high-quality evidence that antimicrobial-impregnated dressings reduce CLABSI rates in critically ill patients compared to other dressings [360]. This systematic review included five trials comparing CLABSI rates after use of chlorhexidine gluconate-impregnated dressings versus polyurethane dressings, and one trial comparing silver dressings to polyurethane dressings. Insufficient evidence supports recommending one antimicrobial-impregnated dressing type over the other.

It is a common burn center practice to incorporate the VAD dressing into the burn dressing in circumstances where VAD insertion needs to go through burned tissue [281]. Currently, an evidence gap exists regarding the most appropriate dressing to use in these circumstances, particularly in the 21st century setting where early surgical debridement of burn wounds and more sophisticated and diverse vascular access techniques, devices, and dressings are employed. Based on the findings of one small trial, topical mupirocin applied around the insertion site may be considered when catheters are inserted through burn wounds, but it needs to be applied three times a day for optimal effect [295]. The magnitude of benefit and potential harm through selection of microbial resistance should be examined in a larger study before this strategy is routinely adopted. Silver dressings appear clinically appropriate, and could also meet the needs of the surrounding burn wound, but this practice is not evidence-based and further research is required to validate the efficacy of this approach. Chlorhexidine gluconate-impregnated dressings are discouraged because of their potential to further impair skin integrity, and standard polyurethane dressings are inappropriate as they provide no protection from contamination and are unlikely to meet the wound care requirements of the surrounding burn. In view of the necessity, frequency, and risks associated with VAD insertion through burn tissue, identification of best practices should be a priority for the international burn community.

When available, chlorhexidine-impregnated dressings should be used as arterial catheter insertion site dressings. A systematic review demonstrated that use of chlorhexidine-impregnated dressings for arterial catheters and CVCs resulted in significant reduction in the relative risks of catheter-related BSI and catheter colonization [361]. Furthermore, a large randomized trial that involved all types of short-term catheters, including arterial catheters, demonstrated a reduction in the risk of catheter-related BSI by 65% when chlorhexidine-impregnated dressings were used compared to standard dressings [362].

We recommend that PIV dressings be sterile, and specific patient and clinician factors and preferences, as well as socioeconomic considerations should inform clinical decisions regarding which type of sterile dressing should be used. A systematic review investigating the ideal PIV dressing showed inconclusive evidence as to whether any one dressing product was better than another for the prevention of phlebitis or accidental removal [363]. A large cohort study found that standard polyurethane dressings were the most commonly used PIV insertion site dressings worldwide [275], whereas, in comparison, sterile gauze and tape dressings were not commonly used, despite a lack of evidence that determines the superiority of either. In some RLS, nonsterile tape was used—an unsafe practice which likely reflects wider economic constraints and limited access to safe health care in these settings. International support is required to influence changes that support safe PIV practices in RLS, to reduce globally the burden of unsafe practices on patient morbidity and mortality.

The frequency of VAD dressing changes is equally controversial, with a recent Cochrane review finding no conclusive evidence regarding the benefits of changing CVC dressings at shorter or longer intervals [364]. The interval did not correlate with BSI incidence, pain or mortality. Nevertheless, widespread agreement supports the assessment of all VAD dressings daily to ensure they are clean and intact; because of the increased chance of infection, dressings should be changed when edges become loose or if moisture accumulates underneath them [260,323,365].

Daily inspection

Assessment of the VAD insertion site should be incorporated into routine handover or rounding processes [325,335]. This provides a structured opportunity in the process of care to

assess dressing integrity as well as the catheter-skin junction site for redness, tenderness, swelling, and/or discharge. These may be signs of infection, infiltration, or venous thrombosis, and where necessary, any abnormal findings can be promptly acted upon.

Accessing VADs

Local protocols should provide clear advice regarding how to access VAD hubs and ports for therapeutic care purposes, as these are potential sites for microbe entry. Prior hand hygiene and barrier precaution measures are mandatory, and acceptable disinfectants such as 70% alcohol or >0.5% chlorhexidine in alcohol should be used to disinfect the hubs or ports prior to entry into the intravenous tubing [260,366-369]. Needleless membranes should be used as they are associated with lower rates of CVC-associated infection [370-372].

Replacement

Routine replacement of VADs in burn care remains controversial; evidence and expert consensus is lacking with wide variation in clinical practices and protocols [281]. While some evidence shows that CLABSI rates in pediatric burn patients increase when CVCs are left in place longer than 10 days [367], this evidence is not rigorous. In the broader hospital population, the CDC does not recommend routine catheter replacement as it has not been shown to reduce CLABSI rates [260].

Infected VADs should be replaced, but diagnosis of infection following major burns is complicated by the reduced specificity of fever and elevation of systemic inflammatory markers, both driven by the injury itself. This means that VADs are often replaced unnecessarily on the suspicion of infection. The optimal method for in situ diagnosis of VAD infection remains unclear in the burns setting, but techniques such as paired catheter and peripheral cultures or semi-quantitative insertion site and hub cultures show promise and deserve further research [373].

Using a guidewire to assist with CVC replacement is a recognized technique that provides less patient discomfort and lower risks of mechanical complications [374]; however, it is associated with higher risks of infective complications and as such, we do not recommend using a guidewire to replace CVCs in clinical scenarios where insertion-site infection is present. Similarly, some evidence in pediatric burn patients shows that guidewire exchange increases BSI rates [375].

A recent systematic review showed no differences in rates of infective and mechanical complications between routine PIV replacement at 72–96 h and PIV replacement determined by clinical indication [376]. This finding has generated a substantial shift from previous recommendations and practices which supported routine replacement. Notably, prospective data across two tertiary health services identified an increased risk of *Staphylococcus aureus* bacteremia associated with PIVs inserted in emergency environments [377]. This increased risk suggests that routine removal of these devices should be practiced favoring replacement with new PIVs that can be inserted under improved clinical conditions and that do not compromise the sterility of the procedure. There are clear advantages associated with the strategy of removal on clinical indication in burn patients, who often have limited available insertion sites, but this strategy must be accompanied by rigorous attention to regular insertion site observation and dressing integrity.

Finally, in regard to the ongoing management of VADs, there are mandatory minimum documentation requirements. These include reporting on the type of VAD used, its length, the agents used to clean and dress the site, tolerance of the procedure, and the assessment of the insertion site. In addition, prospectively documenting the rationale for removal of all VADs is suggested [378]. Comprehensive data collection will help burn centers investigate and report VAD outcomes and will likely assist with hypothesis development and practice improvement initiatives.

6.1. *Balance of benefits and harms*

In many circumstances, particularly in the acute stages of burn injury and in the severely burn injured, vascular access is a non-negotiable requirement in providing therapeutic and often life-saving treatment. Burn centers need to design clear policies and strategies to provide the appropriate prerequisite resources and leadership to create an organizational culture with good risk-perception, situational awareness, and evidence-based practices that produce resilient health care environments where the cumulative risks of BSI are minimized.

6.2. *Values and preferences*

VAD dressing practices vary widely in burn centers, globally and locally [379]. This variation is influenced by socioeconomic factors, the paucity of high-quality evidence both in the burn and broader literature regarding the best dressings to use, as well as the unique challenges burn injuries can create for VAD dressings. In settings where antimicrobial dressings are available, we advise against using standard polyurethane products as CVC dressings in consideration of the greater risk and consequences of CVC contamination, the challenges associated with securing polyurethane dressings due to exudate or sweating, and the absence of securing points in larger burns [360]. In RLS where access to antimicrobial dressings maybe restricted, vigilant attention to other risk-reduction strategies will be required.

Several studies demonstrate the benefits of clustering VAD maintenance requirements into care bundles to allow for a more consistent evidence-based approach [335,379], and maintenance bundle packs are commercially available in some regions. Overall, VAD maintenance requirements should be a focus of performance improvement and quality initiatives.

6.3. *Costs*

Antimicrobial-impregnated dressings are more expensive as consumables than their standard counterparts such as standard polyurethane dressings, but the returns on these outlays are multiplied by the reduction in BSIs and the saving of unnecessary bed days. Health care costs for the ongoing maintenance of VADs are not insignificant, and these costs become substantially greater with the emergence of VAD-related complications. Investment in establishing, implementing and monitoring compliance with VAD maintenance protocols, processes and systems will improve the quality of patient care, patient outcomes and organizational efficiency.

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Recommendation 7

Organizational processes should be in place for surveillance of VAD outcomes.

7. Considerations in formulating Recommendation 7

Increasing the appropriateness of VAD insertion in burn patients should be regarded as a high clinical priority. The target of zero CLABSIs is realistic [348]. Minimizing the number of needle punctures to the skin and the number of VADs used on unique patients, reducing VAD manipulations such as dressing changes and eliminating other clinical breaches in the care of VADs are all worthy pursuits likely to reduce patient complications, LOS, and cost of care. Prospectively collecting data related to these clinical indicators, which are likely to be associated with VAD complications, could assist burn centers in targeting specific quality improvement (QI) initiatives. Surveillance is a well-established QI initiative used to assist in the prevention of BSIs, including CLABSI. Burn centers should collect, analyze and report accurate data regarding CLABSI rates as well as key process indicators relating to VAD failure. These data capture the life-cycle of the catheter from pre-insertion assessment through removal; this facilitates the identification of trends, benchmarking with peers and historical trends, and the prioritization of local infection prevention and other clinical practice improvement initiatives and their impact. Many countries maintain a mandatory legislative requirement for health care organizations to report CLABSI rates [380]. The CDC's National Nosocomial Infections Surveillance (NNIS) system is a standardized method for collecting CLABSI rates and is used internationally [381]. Studies have demonstrated that using this system in combination with infection prevention initiatives has reduced BSI-associated morbidity and mortality [382].

Notwithstanding the rates of CLABSI in the burn population, specific independent risk factors associated with additional VAD complications are not well defined. This knowledge gap should be viewed as an opportunity for local organizational QI processes. Incidents involving CLABSIs and other VAD complications should be critically reviewed, investigated and managed in accordance with local governance processes. Opportunities to learn from adverse events should be taken so that contributing factors can be identified and strategies implemented to prevent their happening again. Furthermore, compliance with insertion and/or maintenance bundles and/or their components, such as hand hygiene, should be audited and reported to the clinical team as part of routine QI processes [335]. Importantly, engaging both the clinical and leadership teams in audit feedback and case reviews, as well as identifying and implementing QI initiatives, will heighten organizational cultural awareness of the risks and burden of CLABSI, BSI, and other VAD-associated complications, and will further improve the safety climate and patient safety.

7.1. *Balance of benefits and harms*

Surveillance of VAD-related complications helps burn centers quantify risks and monitor the efficacy of prevention strategies. Surveillance of BSI, CLABSI, as well as other hospital acquired infection, is usually performed by hospital-wide infection prevention teams. Burn center organizational processes should be in place to allow for at least routine periodical monitoring of compliance with bundles, and/or other insertion and maintenance protocols and procedures. This information is important for burn teams to have a greater situational awareness of local VAD-associated risks, which can lead to QI initiatives that can improve patient safety and to more mindful and safe practices at the patient bedside. Several studies have demonstrated the combined benefits of performing surveillance along with other strategies, including education, bundles and cultural changes, in collectively reducing VAD-related complications [337,383]. As health care professionals are increasingly required to be accountable for the provision of quality care, requirements for surveillance will continue to increase.

7.2. *Values and preferences*

Burn center surveillance methods are usually administered by the overarching hospital organization. Both manual and electronic surveillance options can be used. Manual surveillance systems are human resource-intensive; however in some RLS, manual surveillance methods may be the only option.

7.3. *Costs*

Organizational time and resource requirements for data validation are not insignificant. Electronic surveillance systems linking increasingly sophisticated electronic medical records and patient information systems have been shown to reduce resource requirements [384]; however, at this stage they appear not to be sophisticated enough to reliably manage the complexities of a severe burn admission and to report accurate data [385].

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Metabolic manipulation

Preamble: Metabolic modulation can provide adjunctive benefits to burned patients; however, the dominant concerns of *wound closure* and *nutritional support* frequently become the principal determinants of both overall outcome and metabolic state. As both of these topics are addressed under their own ISBI Practice Guidelines, the authors here wish to reemphasize the importance of early burn excision [386] with durable wound closure [387] and early, adequate enteral nutrition [388] as the primary means of enhanced survival [389], as well as metabolic modulation in the treatment of burns.

Recommendation 1

Maintain core body temperature and endeavor to avoid heat loss in the acute phase for burns involving 20% or more of the total body surface area (TBSA), absent contraindications.

1. Considerations in formulating Recommendation 1

Patients with major burn injuries exhibit an elevation of the hypothalamic temperature set-point [390], and will expend energy to maintain a higher baseline body temperature [391]. Thermal homeostasis results from the balance of endogenous heat (enthalpy) released via the flow of biochemical energy within living structures and released/absorbed from the

environment. Heat transfer occurs via radiation, evaporation, conduction, and convection. Radiative heat transfer occurs through the emission and absorption of infrared photons and is the primary means of heat loss in healthy persons in comfortable environments. Obligatory evaporative heat loss often occurs following burn injury, when normally dry skin is replaced with transudative and open wounds. The rate of evaporation is determined by both the temperature and the humidity at the skin surface; high humidity (vapor pressure) slows further evaporation while dry atmospheres will increase evaporative cooling. Evaporation of 1 mole (18 mL) of water absorbs 40.3 kJ, thus the evaporation of 1 L from a 100 L body of water will reduce the remaining water's temperature by 5.5 °C. Conductive heat transfer occurs by the direct contact between matter, with transfer of molecular kinetic energy leading to the equilibration of temperature between two bodies. The rate of heat transfer depends on the heat capacity and temperature of the matter contacting the burn patient, with wet, saturated dressings and metal surfaces capable of much faster transfer than air, or undisturbed air trapped within dry dressings or blankets which serve as effective insulation. Convection is a special case of the above mechanisms of heat transfer, whereby a flow (air or liquid) of given temperature brings matter to that set temperature. While this provides a comfortable (often dry) environment via modern heating, ventilation, and air conditioning systems, it can rapidly cool an improperly insulated burn patient.

1.1. *Balance of benefits and harms*

The harms of post-burn hypothermia are well-recognized, as it is thought to be a contributor to early mortality. The thermal treatment of two particular populations is unclear: burned patients post arrest with altered neurologic exam and patients with carbon monoxide injury. In these populations, it may be reasonable to allow normothermia (37 °C). Further study is warranted.

1.2. *Values and preferences*

Measures to maintain body temperature are available in nearly all resource settings, including transport vehicles. The burn patient's body temperature should be monitored frequently or continuously, permitting early recognition of disturbed thermal homeostasis.

1.3. *Costs*

Costs to maintain thermal homeostasis range from minimal (that is, for plastic bags and dry sheets/blankets/dressings) to the cost for radiative warming devices (heat lamps) to extensive (purpose-built burn operating suites capable of maintaining temperature above 28 °C and humidity above 60%). While extensive facility modifications may enable the routine care of massive burns, simple measures implemented with a sound understanding of heat transfer principles often remain the most effective. Placing plastic bags over clean/dry extremity dressings and avoidance of wet linens are simple measures that can be employed successfully in all resource settings.

Recommendation 2

Early mobilization, including assisted ambulation, should be initiated as soon as possible after burn injury.

2. Considerations in formulating Recommendation 2

Exercise is a proven modulator of muscle mass after burn injury and has been shown to reduce the need for reconstructive procedures [392], while immobilization causes catabolism. A post-discharge aerobic exercise program should be instituted if resources are available, with the goal of achieving 30–60% of reserve heart rate. This value is obtained by adding 30–60% of the difference between the maximum and resting heart rates to the resting heart rate. The maximum heart rate can be estimated using the formula 220 beats/min minus age in years. This intervention may be implemented across the entire spectrum of health care resources.

2.1. *Balance of benefits and harms*

The potential harms of early mobilization and exercise after burn injury are limited. Graft dislodgment can typically be prevented by use of requisite dressings and operative technique. Recurrent open wounds at mobile surfaces, including auto-release of burn scar contractures, are a symptom of post-burn tissue deficit and attendant functional limitation, not a harm per se of normal activity, exercise, or early mobility. Open wounds should be actively treated to restore functional movement, rather than passively accepted along with immobility and functional loss.

2.2. *Values and preferences*

Some physical activity, such as passive range-of-motion exercises by bedside personnel and early ambulation, once tolerated, can be incorporated in any burn care setting. Dedicated therapists and exercise science professionals can tailor the type, duration, and intensity for each patient's maximal benefit, but ensuring the burn patient's physical activity is a shared responsibility of the burn team.

2.3. *Costs*

Costs for exercise are variable and depend on the additional use of specialized personnel and equipment. Basic range-of-motion and physical activity can be achieved with minimal expenditure.

Recommendation 3

For burns greater than 20% TBSA, caloric requirement should be provided predominantly with carbohydrate and protein, and in accordance with accepted formulae. Pre-injury nutritional status, weight trend, World Health Organization (WHO) growth charts, and indirect calorimetry may be used to personalize this estimate of post-burn caloric needs.

3. Considerations in formulating Recommendation 3

Estimation of caloric requirements and of the nutritional content of feeds can be performed across the entire spectrum of resource constraints. In addition to maintaining body mass, adequate caloric intake improves muscle protein net balance. Provision of caloric needs via carbohydrates [393,394] and protein, rather than fat, maximizes endogenous insulin release to synergistic anabolic effect [395]. Several formulas are available for use.

3.1. *Balance of benefits and harms*

It is clearly recognized that burn patients require protein and caloric intake in comparison to unburned individuals. It is presently difficult, if not nearly impossible, to maintain pre-burn body intracellular mass [396]. Feeding to maintain body mass typically results in fat accretion [397], although whether and to what extent this store supports subsequent growth/remodeling or is deleterious remains unresolved. All efforts should be made to provide adequate calories. Enteral feedings should only be discontinued in the event of intolerance, as demonstrated by abdominal distension, consistent gastric residuals of more than twice the tube feeding volume, and voluminous diarrhea.

3.2. *Values and preferences*

Several formulae, including the Curerri and Galveston [398–402], are available to provide age-, gender-, and body habitus-based estimation of caloric needs. Nutritional prescription may be tailored based on measures and factors which conform to the local practice environment.

3.3. *Costs*

Estimation of caloric needs is within burn-team competencies and need not cause additional expenditure. Formula choice may depend on availability and hospital policy, but reasonable efforts to choose a high-calorie protein formulation should be made within these constraints.

Recommendation 4
In the setting of aggressive nutritional support of burns >20% TBSA, if blood glucose exceeds 180 mg/dL, supplemental insulin should be provided to maintain a target blood glucose of approximately 150 mg/dL.

4. Considerations in formulating Recommendation 4

Although intensive insulin therapy has fallen out of favor due to morbidity associated with hypoglycemic episodes, burn injury and secondary infection do cause profound alterations in glucose flux [403,404]. These alterations are not infrequently associated with significant hyperglycemia above 180 mg/dL. In this setting, it is reasonably safe and appropriate to administer insulin to a target blood sugar of 150 mg/dL. The anabolic effects of exogenous insulin have been amply demonstrated, and it is designated in the WHO Model List of Essential Medicines (http://www.who.int/medicines/publications/essentialmedicines/en/).

4.1. *Balance of benefits and harms*

Although hypoglycemia is recognized as a potential harm of insulin therapy, the present recommendation is made to maximize benefit (treatment of significant hyperglycemia and anabolic effect) and minimize the harm of hypoglycemia (liberal glucose target of 150 mg/dL). If a capability to monitor electrolytes including potassium is unavailable, this uncertainty increases potential harm of insulin treatment of hyperglycemia and treatment should be adapted accordingly to the prevailing resource level.

4.2. *Values and preferences*

Insulin administration should be performed at the discretion of the treating clinician. In patients with large burns on stable feeds with good vascular access and available glucose monitoring, insulin intravenous infusion overcomes the uncertain absorption with subcutaneous injection, but in most patients, subcutaneous injection is acceptable.

4.3. *Costs*

Glucose monitoring and insulin administration is generally possible in most health care settings. Clinician discretion is needed to assess and adapt for site-specific risks/concerns (insulin quality, poor vascular access, or poor accuracy in blood glucose measurement).

Recommendation 5
In burn patients 18 and younger after burn resuscitation, a nonselective beta adrenergic blocker may be given via oral or enteral route to reduce heart rate. Heart rate monitoring (at least pulse oximetry) should accompany dosage titration to achieve 75% of the admission heart rate. Additionally, oxandrolone can be considered as adjunctive therapy to preserve body and muscle mass after burn injury.

5. Considerations in formulating Recommendation 5

Catecholamines are a major mediator of post-burn hypermetabolism [405,406]. Propranolol is listed as a WHO essential medicine, and has been amply demonstrated to modulate post-burn hypermetabolism in children [407]. The clearest evidence indicates a reduction in heart rate, cardiac work, and post-burn hepatomegaly. Additional effects may include beneficial immune modulation. Oxandrolone is approved as adjunctive therapy to promote weight gain after severe trauma, infections, or extensive surgery. In burn patients, there are numerous studies indicating the need for preservation of lean body mass [408,409]. Central hypogonadism is a recognized sequela of burn injury in men [410], and may

represent an additional indication for treatment. Finally, there are some indications of synergy between propranolol and oxandrolone in countering post-burn growth arrest in prepubertal children [411], and in modulating scar formation.

5.1. *Balance of benefits and harms*

Each burn unit must weigh the potential benefits and harms of pharmacologic intervention in their patients. These agents appear to be beneficial in children with large burns, while further generalization awaits multicenter, randomized study. Particular care should be taken in children less than 2 years of age, for whom cardiac output may be heart-rate dependent, and for patients with inhalation injury, as beta blockade has the potential to be problematic. Beta blocker therapy should be delayed in patients who are hypotensive due to inadequate resuscitation until normovolemia is established and hypotension resolved. If oxandrolone is used, liver function studies should be monitored weekly to ensure that there is no increase in transaminase levels, which can occur with oxandrolone therapy.

5.2. *Values and preferences*

Pharmacologic adjuncts may provide additional benefit in burn units where the burn team decides that they can be safely implemented; however, the dominant determinants of metabolic aberration remain nutrition, wound closure, and prevention/treatment of infection.

5.3. *Costs*

Propranolol is widely available (WHO list of essential medications) and the additional cost is modest. Oxandrolone current pricing and regulation may pose barriers to its implementation in some burn units, although others routinely employ this agent.

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Mobility, exercise and physical function

Part 1: Mobility, exercise and physical function—Mobility Recommendation 1

A. *Mobility and ambulation should be initiated as early as possible with burn survivors regardless of the size of burn injury.*
B. *Patients with lower extremity skin grafts should use supportive compression to the legs when mobilizing in upright positions.*
C. *Assistive devices may be used to facilitate mobilization or ambulation after burn injury in order to improve feasibility, safety and independence of mobilization.*

1. Considerations in formulating Recommendation 1

The scientific literature clearly establishes that a patient's confinement to bed and continued inactivity results in significant musculoskeletal problems [412,413], pulmonary and cardiovascular alterations [414,415], and functional decline causing significant physical debilitation [416]. Burn patients experience periods of immobility due to the need for surgery, mechanical ventilation or critical illness. The potential impact of bed rest with this population is exacerbated due to the presence of healing wounds and scar formation, which place a patient at risk for loss of motion and function. In more severely burn injured patients, the effects of bed rest can be worsened by a hypermetabolic response that is characterized by protein catabolism and loss of lean muscle mass and muscle strength [417,418]. In addition, patients have difficulty with ambulation and endurance after burn injury. A study evaluating gait outcomes in burn survivors at 3 months after injury demonstrated decreased functional exercise capacity and significantly lower ambulation speed in patients with burn injury compared to age-matched normal subjects [419]. Even when other physical outcome measures improve, functional exercise capacity and lower limb function remain significantly reduced at 6-12 months after injury or longer [420]. Burn survivors who were interviewed at least 3 years after their injury, and up to 30 years post burn, reported "problems with walking or running" as the second most frequent musculoskeletal problem since their injury (64% of burn survivors) [421].

Recommendation 1 promotes early mobility in terms of advocating for whole-body postural changes and limb movement, including range of motion (ROM) with progression toward ambulation or goal-directed propulsion (if the patient is non-ambulatory). In patients with significant and extensive burn injury and critical illness, a barrier to early mobilization is patient safety including physiologic instability and medical device removal. Nydahl et al. conducted a systematic review of critically ill patients in the intensive care unit (ICU) and a meta-analysis of 7500 patients receiving 22,000 mobilization/rehabilitation sessions [422]. The authors concluded that early mobilization and rehabilitation in the ICU can be conducted safely. They reported only a 2% cumulative incidence of potential safety events, and of those, only 0.6% had medical consequences. A retrospective cohort study, including burn and trauma patients who received an early mobilization protocol, also demonstrated that early mobilization was safe and effective [423]. In that study, the early mobility group was less likely to develop pneumonia, deep vein thrombosis, or airway, pulmonary or vascular complications as compared to patients who received usual care. Research evaluating the effects and benefits of early mobility in more severely burned patients is limited as compared to that evaluating patients with less extensive burn injury. However, current evidence suggests that when mobilization and ambulation are initiated early and bed rest is minimized, burn patients have improved outcomes. Deng and colleagues, evaluating only burn patients, studied the impact of switching from a passive training protocol, which included anti-contracture positioning, passive ROM exercises, splinting, and prolonged strict bed rest time, to a more active mobility training protocol that emphasized active ROM, upright positional changes, transfer training, progressive ambulation and less strict bed rest. The authors found that the mobility training cohort had shorter hospital and burn intensive care unit (BICU) stays, and improved ROM in many joints [424]. Okhovatian and Zoubine implemented and compared early rehabilitation and ambulation of burn survivors with less active routine practice and found the group who received the early rehabilitation intervention had significantly fewer burn contractures [425]. Further investigation of early mobilization and ambulation with extensively injured burn patients is needed to provide information about the most beneficial methods, types and dosage of interventions for these patients.

Recommendation 1 addresses the early mobility of severely burn-injured patients as well as patients with smaller and less extensive injury. Immobilization in a non-critically ill and less extensively injured burn patient is typically implemented out of concern for skin graft loss. However, evidence suggests that early mobility after skin graft surgery does not put the graft at greater risk and may result in improved outcomes [426]. In a prospective randomized controlled trial of early ambulation after autografting, Lorello et al. found that patients who received ambulation training within 24h postoperatively had no difference in graft loss, more minutes of ambulation during hospitalization, and less graft-site pain compared to those who were on bed rest for 5 days. Evidence specifically addressing early ambulation after lower extremity skin grafting was reviewed to develop practice guidelines that could be used with burn survivors. The final recommendation from a systematic review of 16 research studies and a subsequent expert consensus exercise stated that an early postoperative ambulation protocol should be initiated as soon as possible after lower extremity grafting [427]. All of the studies in the systematic review performed by Nedelec et al. detailed some sort of supportive compression application with ambulation. Therefore, this specific recommendation is added to the current guideline for mobilization.

The use of assistive devices or ambulatory aids with burn survivors is not well studied; however such devices are widely

used in clinic settings to help mobilize patients and are therefore included in this recommendation. Various devices such as crutches, walkers, orthosis, tilt tables, etc., have been used to facilitate early mobility, independence and maintenance of physiologic and psychological parameters [428]. Such devices may allow mobilization and ambulation to be conducted earlier, with greater safety to the patient and less physical burden on the practitioner [429,430]. Practitioners should only use such devices to promote rehabilitation goals [431] and be cautious of the prescription of devices that may complicate recovery such as crutches with a foot burn that could promote swelling and reduce ankle ROM. About 23% of burn survivors reported that they used an assistive device after their injury [421]. The goal of mobilization is to help a patient return to a pre-burn level of function or the highest possible level of independence. Therefore, the type of device selected and a plan for discontinuing use of the device should be considered upon initiation of the device.

1.1. *Balance of benefits and harms*

Immobilization and bed rest after burn injury can lead to further complications and prolonged hospitalization. Early mobilization, on the other hand, may mitigate some of the known complications from bed rest and extensive burn injury. Potential risks with early mobilization include loss of skin graft integrity as well as decreased physical safety and medical stability. However, the evidence described above, in both critically ill patients and burn patients specifically, suggests that this risk level is very low and may be overestimated clinically. The benefits of early mobilization for the burn patient include but are not limited to decreased length of hospital stay, improved ability to ambulate and reduced scar contracture rates. While early mobility and ambulation training is recommended, evaluation of each individual burn patient's medical and surgical status, complications, and comorbidities must be considered when determining optimal timing, manner and progression of the intervention. Safety of the patient is a priority and should be assessed by the burn team prior to initiating mobilization therapies.

1.2. *Values and preferences*

A burn team must work to develop a "culture" of consistent communication and reinforcement of early mobility and ambulation where the roles and responsibilities of all team members are determined and coordinated [432]. This is especially important in resource-limited settings (RLS) where access to modern equipment and sufficient staffing may be limited. The role of early mobilization may fall on any ancillary team member, a family member, or the patient him/herself. Education regarding the potential benefits, safety measures and alternate use of basic equipment (chairs and beds) should be provided early in the course of care.

1.3. *Costs*

Mobilization at an early stage of recovery, when a burn patient is more dependent with movement and function, may require specialized equipment or increased personnel, which has a financial cost. Given that many studies show a reduced length of stay and subsequent cost savings with early mobility [433], the cost of increased staff or equipment is unlikely to be outweighed by the potential overall increased cost of providing care for a longer time. Cost to the patient with less time in the hospital and a potentially sooner return to work may reflect a cost savings that is not yet fully captured in the research.

Part 2: Mobility, exercise and physical function—Exercise Recommendation 2

Burn survivors should follow exercise programs including range of motion, strengthening and cardiovascular exercises.

A. ***Exercise programs should be implemented for a minimum of 6 weeks and continued until pre-burn motion, strength and endurance are achieved when possible.***
B. ***Exercise programs show benefit to the burn survivor when initiated as early as discharge from acute care but may have benefit if implemented sooner.***
C. ***Physiologic response of the burn survivor to exercise should be monitored during exercise performance.***

2. Considerations in formulating Recommendation 2

Studies have shown that after burn injury, patients experience significant loss in joint motion [434,435], muscle strength [436] and cardiovascular endurance [437]. These deficits may persist long after injury and stay below the levels seen in age-matched individuals from a normal population [421,438,439]. A systematic review of physical fitness in people after burn injury concluded that exercise training programs can result in relevant improvement in all components of fitness [440]. A rehabilitation summit conducted in 2009 involving 20 clinicians with expertise in burn rehabilitation determined that exercise is a fundamental part of burn rehabilitation [441]. Exercise programs should maintain or restore ROM, improve muscle strength and endurance, improve balance, coordination and proprioception, promote wound healing, and restore the patient to the premorbid level of functional independence when possible. Allied health practice guidelines established in 2014 emphasized that the optimal burn rehabilitation exercise program includes individualized education, effective pain relief, and appropriate psychosocial support to motivate adherence with the program [442].

Range-of-motion activities are a central component of any exercise program after burn injury [443]. Multiple studies have shown that joint contracture is a significant problem for burn survivors due to scar formation that occurs during wound healing and involves the dermis or deeper tissues [434]. A systematic review of the prevalence of burn scar contracture reported a 34–58% incidence at discharge from the hospital [444]. One study showed that the amount of scarring in the skin area associated with movement at a particular joint (the shoulder in this case), negatively correlated with ROM recovery as measured by goniometry and during functional tasks [445]. Exercise is one of the most used modalities in rehabilitation of burns throughout the world [446]. Neugbauer et al. showed that a 12-week music and exercise group program provided to

children with burn injuries resulted in significant improvement of ROM in more joints than standard care alone [447]. ROM exercises after burn injury may be performed passively, actively or with active assistance and due to the influence of collagenous scar tissue, it is recommended to provide low load, long duration forces to achieve full ROM [448,449].

Significant burn injury also results in muscle wasting [450], muscle weakness [451], less muscle torque, work and power [452], limited balance [436], and greater levels of fatigue [453]. Studies in adults and children have shown that the implementation of exercise programs after burn injury can improve aerobic capacity [453], functional outcomes [454], lean body mass [455], mobility [456], pulmonary function [457], peak muscle torque [458], strength [459], and total work volume [460]. A systematic review of 20 studies, 14 of which were randomized controlled trials, resulted in the recommendation that burn survivors who test below normal levels of strength and cardiovascular endurance should be prescribed a supervised resistance and/or aerobic exercise program [461]. Therefore, Recommendation 2 includes strengthening and conditioning exercises for the burn survivor. The bulk of evidence on the benefits of strengthening and cardiovascular training concerns severe burns with a total body surface area (TBSA) burn of greater than 30%. However, some evidence suggests that nonsevere burn injury has significant effects on cardiovascular function and long-term morbidity in some burn survivors, suggesting that further investigation of the impact of early exercise with this subpopulation is needed [462,463]. An exercise program is generally initiated upon admission to the hospital, continued until discharge, included in outpatient care, and continued independently at home until full recovery can be achieved when possible. Based on current studies which inform Recommendation 2, there is known benefit to burn survivors if exercise is initiated upon discharge from acute care and continued for at least 6 weeks. However, a paucity of studies evaluate earlier intervention or longer durations of treatment despite the typical clinical approach to initiate exercise, in particular ROM exercises, immediately following burn injury. Therefore, clinical practice suggests exercise implemented early in the course of recovery and continued until premorbid status is achieved may be beneficial for the individual burn survivors and was added to the recommendation.

Most studies investigating exercise with burn survivors advise supervision of subjects by an exercise specialist or rehabilitation therapist and provide careful monitoring of the patient's response to exercise [457,461,464]. Monitoring cardiovascular and pulmonary responses while introducing and progressing exercises with a medically compromised patient is essential for safety and thus added to this recommendation for clarity. In addition, monitoring patients for hyperthermia during exercise is important due to evidence that burn survivors have greater intolerance for exercising in heated environments [465]. Measuring a patient's response to exercises can be achieved with a variety of methods such as goniometry or patient-reported perceived exertion, which allow for objective quantification of progress [466,467]. Instruction to the patient and family on how to monitor physiologic response to exercise should be provided as the patient gains independence with exercise at home.

2.1. *Balance of benefits and harms*

The body of knowledge on the benefits of exercise in adults and children after burn injury is significant. As with the general population, people will vary with their capacity, tolerance and response to exercise. Therefore, exercise programs initiated with burn survivors should be individualized to the specific needs of the person, supervised to ensure adequate performance and progression until independence is achieved, and monitored for safety and tolerance. Exercise programs should never interfere with medical care or compromise a patient's medical stability, health or wellness.

2.2. *Values and preferences*

With the growing evidence that exercise benefits burn survivors, the value of integrating such programs into current burn care may enhance the overall recovery from burns. Individual assessment of the patient's impairments and functional deficits should be performed to develop a customized exercise program specifically addressing the deficits. The type and intensity of exercises at the various stages of recovery after burn injury may vary depending on the patient, the burn injury, subsequent complications, and psychosocial factors. The pace, duration and frequency of the exercise program may need to be varied between patients in order to provide maximal benefit and safety, but ultimately the goal of full premorbid level of recovery should be common to the majority of patients surviving burn injury.

Previous practice guidelines have included recommendations regarding positioning and splinting of the burn patient [468]. These modalities are important to counteract the contractile forces of scars after burn injury. Active exercises that promote motion, strength and endurance must be balanced with positioning and splinting for contracture management and optimal functional outcome.

2.3. *Costs*

Exercise principles can be applied with expensive equipment or no equipment at all and can be guided by a knowledgeable and skilled professional or performed independently. Although the recommendation includes initial supervision and guidance for the development, implementation and progression of an exercise program, establishing good communication with and thorough education to patients should help them gain independence and sufficiently perform their prescribed exercises in a home setting. Exercises can be designed to use only body weight or activities in a natural environment. If weights are needed, various easily accessible items can be adapted for use (e.g., bags of rice or sand, cans of food, etc.) In RLS, therefore, to appropriately integrate exercise into rehabilitation after burn injury, knowledge of the benefits of creative methods of implementing exercise is of greater importance to the burn clinician than is any specific equipment.

Part 3: Mobility, exercise and physical function—Physical function

Recommendation 3

Burn survivors should receive rehabilitation for restoration of function with the goal of achieving premorbid functional status when possible.

A. *Evaluation and treatment planning of functional limitations should be guided by the domains of the World Health Organization's Conceptual Framework of the International Classification of Disability and individualized to the burn survivor's needs.*
B. *Appropriate functional outcome measures should be used to document and monitor a burn survivor's progress and outcome.*
C. *For optimal functional outcomes, a multidisciplinary burn team approach should be used and physical rehabilitation should include occupational and/or physical therapy initiated upon admission and continued throughout recovery.*

3. Considerations in formulating Recommendation 3

Patients are surviving more severe burn injuries than ever before and as a result have complex rehabilitation needs [441]. Physical function or a person's ability to perform activities of daily living, instrumental activities of daily living and productive activities such as school and work can deteriorate significantly after burn injury. The World Health Organization's (WHO) framework of International Classification of Functioning, Disability and Health (ICF) identifies three levels of functioning: body or body part, the whole person, and the whole person in a social context. Changes after burn injury can affect one or all of these levels resulting in impairments, activity limitations and participation restrictions [469,470]. Deficits in function occur rapidly after burn injury with peak decline occurring as early as 3 months post injury [471] and remaining significantly reduced for months or even years after injury [420,421]. Ryan et al. found lower levels of physical function recovery were associated with increasing burn size [472]; however functional deficits can be seen in patients with both small and large burns [473].

Recommendation 3 supports the implementation of rehabilitation using a variety of techniques and tools available to rehabilitation clinicians with the goal of restoring a patient's function. Return to premorbid levels of function, or better, is possible for most burn survivors, however there are some circumstances (e.g., post-burn amputations, irreversible neuropathies, developing child, etc.) where achieving the greatest level of independence is an alternate goal. Although limited evidence addresses the impact of many specific rehabilitation techniques with the burn population, a comprehensive review of the burn literature was conducted and found general support for rehabilitation treatment after burn injury [473]. Using a multidisciplinary burn-team approach for rehabilitation to help restore physical and psychosocial function and to regain independence with reintegration to work and society is a well-established component of burn recovery in most burn centers [446,474,475]. Despite studies that report short- and long-term functional deficits in patients post burn injury, studies also demonstrate that many patients can achieve full functional recovery when provided with comprehensive and coordinated care including rehabilitation services [471,476]. Providing an early and aggressive comprehensive rehabilitation program to burn survivors has been shown to reduce patients' length of stay without increased morbidity, result in a more rapid recovery of function, improve resource utilization, increase patients' capabilities with activities of daily living and elevate quality of life [475,477–479]. When inpatient rehabilitation is not possible or is limited, intensive outpatient rehabilitation programs have resulted in reduced costs and quicker return to work for burn survivors [480]. Small burns in highly functional body areas (e.g., hands and mouth) may require rehabilitation; and larger, more extensive burns almost always require some degree of rehabilitation [476,481]. In a prospective, observational multicenter trial in the United States, Richard et al. reported that burn patients received direct rehabilitation treatment approximately 81% of the total acute-care days they were hospitalized for 61.5 min per day [482].

The WHO ICF is a multilevel framework that can be used to guide the burn clinician when evaluating patients after a burn injury and creating a treatment plan for rehabilitation. A summary paper on the state of the science in burn care describes the WHO ICF framework as one of the main recent advances in disability research [483]. Grisbrook et al. detailed the use of the ICF framework to describe a complex burn survivor's functional recovery following injury [484]. The ICF framework can be useful in a variety of settings and within many different cultures because it takes into account the interaction between the described health conditions and contextual factors such as environmental factors (external) and personal factors (internal). A treatment plan after burn injury should be aimed at improving the patient's health status with consideration of patient-specific contextual factors. In addition, the framework allows for the individual patient to participate in the development of his/her own treatment plan and to customize it to specific needs and desires.

Recommendation 3 also advocates for functional outcome measures to be used at various phases of recovery to assess a burn survivor's functional recovery. Measuring outcome as it relates to various aspects of function (physical, psychological, social, etc.) has utility to the clinician and to advancing the overall knowledge base in burn care. Outcome data enable the clinician to determine efficacy of treatment, objectively monitor the patient's progress, make necessary interventional modifications, and provide the patient with feedback about recovery. On a broader level, utilizing outcome measures helps determine and maintain standards of care in burn care and rehabilitation and facilitates a more common language for the interpretation of research or treatment advances [485]. A myriad of available outcome measures may be used to evaluate outcome on any of the WHO ICF levels and some have been developed specifically for the burn population [486–488]. However, currently there is no one test or battery of tests that is used consistently across burn centers. Falder et al. broadly adapted the WHO model to propose seven core domains of outcome assessment for burned adults as a preliminary framework for collaboration among burn centers, and a modular minimum outcome measurement framework has been further developed [485,489].

Functional recovery involves more than physical rehabilitation and for gauging reintegration back to society should include psychological rehabilitation and social support, which are addressed in other areas of this document. A multidisciplinary approach to the rehabilitation of burn survivors has shown to result in functional improvement regardless of TBSA,

age or premorbid psychological status [490]. Comprehensive burn care requires a team approach with all burn professionals contributing their specific expert knowledge and skill. Occupational and physical therapists, who are professionally trained in the remediation of impairments, activity limitations and participation restrictions, are best suited to provide physical rehabilitation services to burn survivors due to their training and skill with the many aspects of functional recovery. Paratz et al. demonstrated that a high intensity cardiovascular or resistance-training exercise program provided by rehabilitation experts significantly improved functional, physical and psychological outcomes compared to a self-directed rehabilitation program [491]. Providing therapy services has also resulted in improved mobility and greater patient-reported satisfaction with care [492,493]. Not all burn centers in the world have professionals with training in occupational or physical therapy. However, for those that do, these professionals should deliver physical rehabilitation services. A core set of competencies have been established to guide burn therapists in the delivery of rehabilitation services and includes multiple domains of practice [494]. In settings that do not have access to trained therapists, specific staff should be identified and trained on basic rehabilitation techniques and should be responsible for their implementation. Li et al. designed a rehabilitation intervention model for burn patients using multiple team members focusing on rehabilitation, and that included patient involvement. They found that patients who received training using this rehabilitation model had significantly better scores for various outcomes including physical function when compared to patients who received conventional care [495].

3.1. *Balance of benefits and harms*

Rehabilitation is another component of care that may require additional effort, time and burden to the patient and the patient's family. Rehabilitation can be painful and difficult. However, the recovery of function or implementation of functional adaptions to reduce activity limitations and facilitate participation by reintegrating burn survivors into their family, work or school and community will ultimately reduce the long-term burden on society. Using a structured and measurable framework for the delivery of services, regularly measuring the efficacy of interventions provided, and using a multidisciplinary approach with trained professionals providing rehabilitation can improve the overall outcome and experience of burn survivors.

3.2. *Values and preferences*

Functional recovery includes physical recovery but must always be considered in the context of multiple other factors that influence recovery such as pain and psychosocial adjustment and social support. In RLS, comprehensive rehabilitation is acknowledged as an important part of an ideal recovery process, but the resources to provide such services are often limited [446]. Volunteer burn organizations or cooperative educational efforts between burn centers may be used for burn specific training opportunities in countries where rehabilitation education and training are limited. Clinicians providing rehabilitation services should exercise critical thinking in the most economical and beneficial means of providing treatment as well as be innovative and creative in the implementation of specific strategies to maximize available resources.

3.3. *Costs*

Rehabilitation personnel to provide therapy for recovery of physical function results in a personnel cost to the patient, the burn center and/or the health systems. If burn survivors are not provided rehabilitation services, activity limitations and participation restrictions may prohibit their ability to return to work and minimize their financial contribution to society [496]. The costs of providing rehabilitation services must be weighed against the potential societal burden of the increased number of disabled citizens.

Some outcome measures may incur costs associated with purchasing tools, administrative assistance or scoring. In RLS, rehabilitation professionals are often available but lack the resources to provide many needed therapeutic interventions and assessments [446]. Burn clinicians should use the tools available to measure outcomes as objectively and consistently as possible and monitor the results of the interventions they provide. Many tools are available online for free or minimal cost and require very little training (https://www.sralab.org/rehabilitation-measures).

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Pain control

Preamble: Although no single treatment standard exists for burn pain management, comprehensive pain management protocols can be helpful in treating pain. This guideline addresses pain management only. Practitioners should integrate this guideline with those addressing anxiety and delirium as well as other Psychiatric Disorders, which appear in other sections of this document (p. xx).

Recommendation 1

Pain related to burns is a complex combination of distress, anxiety, delirium, and situational and emotional factors. Management, monitoring, and treatment of pain are central to optimizing outcomes following burn injury.

1. Considerations in formulating Recommendation 1

The experience of pain in burn patients is complex and the effects are both physiologic and psychological [497]. Clinical data indicate that both short- and long-term physiologic and psychological benefits accrue from good pain control [498]. Prolonged, poorly managed acute pain has been associated with negative outcomes including a reduction in quality of life, poor physical functioning, increased incidence of chronic pain, suicidal ideation, and poorer general and mental health status. Significant symptoms of post-traumatic stress disorder (PTSD) develop in up to a third of burn survivors and may in part be treatment-related [499]. Good pain control may reduce PTSD incidence [500]. Qualitative studies have reported that patient satisfaction is closely related to their pain experience/management and those with uncontrolled pain report it as the worst pain they have ever experienced.

1.1. *Balance of benefits and harms*

Both short- and long-term psychological benefits accrue from good control of burn pain. Rates of acute and post-traumatic stress may be reduced. However, all medications have adverse effects, and practitioners should be aware of and monitor for those effects. Alterations in medication choice or route may be necessary based on patient physiology.

1.2. *Values and preferences*

Eradicating burn pain is not possible, but patients, families, and staff all benefit when burn pain is safely minimized. The type of agent(s) or method(s) used for pain treatment will often be dictated by local customs and resource availability. However, each facility that cares for burn patients should have the ability to provide patient analgesia in some form, preferentially utilizing multimodal therapies. Pain should be addressed both in the hospital setting and in the treatment of outpatient burns.

1.3. *Costs*

The cost of pain management in burn injury will depend on the environment, culture, and availability of any given agent. Patients with well-controlled pain have reduced long-term psychological issues, which can decrease overall societal costs.

Recommendation 2

Monitoring the adequacy of pain control is facilitated by routine use of scoring systems during all phases of care. Scales based on patient self-report are preferred when possible. Validated pain behavior observation-based scales are useful when the patient is unable to self-report because of mental status impairment or young age.

2. Considerations in formulating Recommendation 2

Optimal pain management requires both taking repeated measurements to assess pain and responding to initiated therapy using validated tools. Several pain measurement instruments have been developed and validated for adults and children, including preverbal children [501,502]. Table 3 provides a list of pain assessment tools based on the developmental age of the patient for which they are being used. Monitoring of the degree of pain and the adequacy of control in individual patients is best done using such tools [503,504]. Vital signs alone (heart rate, blood pressure, etc.) should not be used to assess or grade pain, but they may prompt the practitioner to investigate the level of pain with objective scales. Accuracy of pain control is enhanced, and complications may be reduced through avoidance of overmedication [505]. Furthermore, setting individualized goals for effective pain management (e.g., identification of a numeric rating to achieve during wound care) is another important aspect of this recommendation. This accuracy and individualization requires discussion with the patient.

2.1. *Balance of benefits and harms*

Accurate measurement of burn pain may facilitate administration of minimum effective doses which will minimize medication-related complications. Pain tools must be appropriately applied; hence, staff training is essential.

2.2. *Values and preferences*

Monitoring and adjusting therapy to optimize pain control will benefit patients by avoiding under- or overmedication for burn pain. Patients will also value inclusion in discussions of their pain management plan. Every tool listed in Table 3 is available in English; not all have been translated and validated in other languages.

2.3. *Costs*

Use of minimum effective medication doses will facilitate cost control. Some of the tools listed in Table 3 may require purchase while others are free of charge and can either be photocopied for noncommercial clinical use or do not require a written format.

Table 3 – Pain assessment tools.

Age group	Assessment tool	Type of tool[a]	Reference (s)
Pre-verbal children	Faces, Leg, Activity, Cry, Consolability (FLACC) Pain Scale	OB	[506,507]
	The Pain Observation Scale for Young Children (POCIS)	OB	[508–510]
	COMFORT Behaviour Scale (COMFORT-B)	OB	[511]
Children; with cognitive impairment	Revised FLACC	OB	[512,513]
Noncommunicative children (intubated and ventilated)	COMFORT-B	OB	[514]
Verbal children; pre-school age	Faces pain scale revised (FPS-R)	SR	[515]
Verbal children; school age	Faces pain rating scale (FPS-R)	SR	[516]
	Wong-Baker Faces Scale	SR	
	Oucher Scales	SR	
Communicative adults	Visual Analog Scale (VAS)	SR	[517,518]
	Numeric Rating Scale (NRS)	SR	
	Verbal Rating Scale (VRS)	SR	
	FPS-R	SR	
Non-communicative elders	Pain Assessment in Advanced Dementia (PAINAD) Scale	OB	[519]
	Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC)	OB	[520]
	Rotterdam Elderly Pain Observation Scale (REPOS)	OB	[521]
	DOLOPLUS-2	OB	[522]
Intensive care patients	The critical care pain observation tool (CPOT)	OB	[523]
Intensive care patients	Behavior Pain Scale	OB	[523]

[a] OB, observational/behavioral; SR, self-reporting.

Recommendation 3

Pain management should address background, breakthrough, procedural, perioperative, and chronic long-term pain.

3. Considerations in formulating Recommendation 3

The experience of pain varies greatly between clinical states, from the time of injury through long-term recovery. Acute, chronic, background, breakthrough, procedural, and perioperative requirements vary, and pain management strategies must accommodate these differences to provide optimal control [524]. Clearly elaborated interventions appropriate to each requirement will facilitate management [525,526].

Acute pain generally has a sudden onset, is severe in intensity, short-lasting, and felt immediately following injury. Acute pain is frequently the result of tissue injury (such as burn injury) stimulating nociceptors and generally disappears when the injury heals. Types of acute pain include procedural pain (dressing changes) and perioperative pain. Background pain, which is low-level pain but causes persistent discomfort, is likely due to unhealed wounds and other injury factors. *Breakthrough pain*, which is a temporary increase in the severity of pain over and above pre-existing baseline pain levels, is usually intermittent, of sudden onset, severe, and of short duration [527]. *Chronic pain* extends beyond the expected healing time. Chronic pain may begin as acute pain, which then persists for long periods or recurs due to persistence of noxious stimuli or repeated exacerbation of an injury. Different agents are likely required to treat each type of pain. Application of the pain ladder, which emphasizes the use of non-opioid agents for initial treatment of mild pain with step-wise addition of other agents as pain severity increases, is recommended [527].

3.1. *Balance of benefits and harms*

Burn pain is not static. Although background pain does exist, the level of pain varies with interventions. Addressing each of these elements will facilitate safe pain control. Different agents may be appropriate for different types of pain; hence, appropriate identification of pain type and severity is important to obviate over- or undermedication.

3.2. *Values and preferences*

All components of pain deserve treatment, from the acute through the chronic state, with appropriate interventions designed for procedures. The precise methodology of pain control will vary with the resources available in any given setting. However, all burn centers should have pain control capabilities.

3.3. *Costs*

Accurate pain control is likely to be the most cost-effective and will help avoid complications and distress associated with under- and overmedication. Cost associated with medication administration can be offset by patient benefits, including early mobilization.

Recommendation 4

Although opioid analgesics are frequently used in the management of severe acute burn pain, non-opioid analgesics, nonsteroidal anti-inflammatory agents, and nonpharmacologic maneuvers are effective agents in treating burn pain. An individualized multimodal approach to burn pain management that utilizes agents from different classes should be considered.

Important note:
Each patient should be evaluated individually, but development of detailed unit-specific protocols will reduce complications associated with the use of multiple agents and will optimize outcomes. The following options/strategies may be beneficial as adjuncts in pain treatment:

- Dissociative drugs such as ketamine: control of procedural burn pain
- Dexmedetomidine and other non-opiate analgesics: reduce acute opiate requirement
- Non-opioid analgesics, nonsteroidal anti-inflammatory agents, and nonpharmacologic maneuvers: an important adjunct as well as primary therapy for burn pain

4. Considerations in formulating Recommendation 4

Several studies have demonstrated the opiate-sparing effects of combined pharmacotherapy for pain [528,529]. Opiate and benzodiazepine synergy for pain control is well established. Newer agents, particularly the centrally acting alpha-adrenergic agonist dexmedetomidine may reduce opiate needs without exacerbating respiratory depression [530,531]. Approaching each patient as an individual within a regularly reviewed unit-specific protocol will facilitate safe practice [532]. Although insufficient data support a single treatment standard for pain management in the burn patient, guidelines to be incorporated into unit-specific protocols have been published and provided the following guidelines [533]:

- All burn centers should have an organized approach to the treatment of burn pain that considers background, procedural, and breakthrough pain.
- The objective should be for the patient to be awake and alert but comfortable.
- Pain should be differentiated from anxiety.

4.1. *Balance of benefits and harms*

No two patients will have the same experience of pain. Safely leveraging the synergies between drug classes is likely to allow for optimal pain control with reduced medication complications. Using multiple modalities also can potentially reduce the dependence on any single agent.

4.2. *Values and preferences*

The experience of burn pain is not uniform. Individualized management is likely to lead to optimal results. The availability of different agents will likely vary between centers, and clinicians will likely have different agent preferences based on patient and physician experience. Drug shortages may impact drug utilization.

4.3. *Costs*

While new classes of drugs may have a higher per-unit cost, their use may reduce overall pharmacologic needs. The overall cost of the agent must be balanced against drug efficacy and the potential to improve patient outcomes.

Recommendation 5
The impact of emotional factors associated with burn injury and its management should be considered when managing post-burn distress.

5. Considerations in formulating Recommendation 5

Psychiatric illness may precede or be exacerbated by the experience of burn injury [534]. Numerous emotional and psychiatric issues, particularly anxiety, may impact the individual experience of burn pain and should be considered when managing burn associated distress [535]. Opiate pharmacotherapy alone is relatively ineffective in addressing these issues. The addition of psychiatric evaluation and intervention is likely to have an opiate-sparing effect on the experience of burn pain in many patients [536]. For further details on psychiatric and anxiety issues please see the Psychiatric Disorders (p. xx) and Sedation (p. xx) sections of this document.

5.1. *Balance of benefits and harms*

Psychiatric disease is prevalent at a moderate rate in the general population and may be exacerbated by the experience of burn pain. Management of concomitant psychiatric disease may reduce overall pain medication requirements and complications.

5.2. *Values and preferences*

The experience of burn pain may be favorably modified by acknowledging and managing concomitant psychiatric disease. The type of therapy may be dictated by local cultural norms, medication availability, and physician experience.

5.3. *Costs*

The cost of pain pharmacotherapy may be reduced by managing concomitant psychiatric disease. Behavioral modification and nonpharmacologic therapies for psychiatric illness and anxiety may reduce medication costs.

Recommendation 6
Neuropathic sensory changes can contribute significantly to post-burn distress and should be considered and treated in post-burn pain management.

6. Considerations in formulating Recommendation 6

Neuropathic pain is a complex phenomenon that has been poorly characterized physiologically but has a major impact on the experience of burn pain [537]. Gabapentin or pregabalin are more effective than opiates for neuropathic pain and may facilitate improved pain control in selected patients [538]. This

effect may be seen in both the acute and later phases of care [539].

6.1. Balance of benefits and harms

The use of gabapentin or pregabalin may mitigate the experience of burn pain while reducing overall medication needs, thereby minimizing medication-related complications. Agents for neuropathic pain treatment have recognized side effects, which must be taken into consideration when prescribing these medications. Known side effects of gabapentin include sleepiness, dizziness, fatigue, difficulty walking, visual changes (such as double vision), tremor, weight gain, and indigestion or nausea.

6.2. Values and preferences

Addressing concomitant neuropathic pain may improve the management of pain related to burn wounds. The agent used and the techniques applied will be dependent on local resources and drug availability.

6.3. Costs

Addressing concomitant neuropathic pain may reduce the amount of pain pharmacotherapy required. Neuropathic agents are available even in many resource-limited settings (RLS). However, the cost may be prohibitive in certain situations.

Recommendation 7
Nonpharmacologic techniques should be considered as important additional elements of a comprehensive post-burn pain management plan.

7. Considerations in formulating Recommendation 7

Pain cannot be eliminated entirely [540]. Nonpharmacologic treatments such as education, distraction, activity-based play therapy, relaxation, guided imagery, music therapy, hypnosis, acupuncture, enhanced patient control, somatosensory approach of motor imagery, meditation and parental participation all have potential individual utility in facilitating control of burn pain in the conscious patient [541–544]. When patient education is required for optimal use of nonpharmacologic adjuncts, it should be provided when the patient is awake and comfortable, to facilitate understanding. Attempting to instruct the patient during periods of high pain or anxiety is often unsuccessful.
Modification of procedures that induce pain should also be considered when developing an individualized approach to pain management (e.g., change in topical treatment strategies to reduce frequency of dressing change, change timing of dressing change). Each intervention will require individual consideration.

7.1. Balance of benefits and harms

Nonpharmacologic interventions combined with pharmacotherapy may improve the experience of burn pain. With nonpharmacologic strategies for procedural pain control the greatest efficacy is realized once pharmacologic management is optimized.

7.2. Values and preferences

Various nonpharmacologic interventions for burn pain exist. When selecting a nonpharmacologic intervention for patients with burns, considerations include simplicity, easy of learning, immediate usability, and minimal expenditure of time and effort during use. Nonpharmacologic treatments are likely to be successful when accurately targeted to patient developmental age and preferences. Some nonpharmacologic therapies have limited resource needs. Hence, they should be available in virtually every burn center.

7.3. Costs

The application of nonpharmacologic interventions may reduce the amount and cost of medications required for successful management of burn pain. However, certain nonpharmacologic strategies may incur an investment in personnel training and/or equipment. Nonpharmacologic interventions may be particularly helpful in the outpatient or RLS in which availability of drugs or monitoring is limited.

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Sedation

Recommendation 1

Anxiety and agitation occur frequently in the burn patient and are associated with adverse clinical outcomes. Administration of sedatives to burn patients may be required to treat agitation and anxiety.

1. Considerations in formulating Recommendation 1

Burn patients are subject to agitation and anxiety due to the injury itself, the loss of personal property, inability to communicate, and loss of control during procedures and dressing changes. Agitation and anxiety in burn patients is multifactorial, and symptoms manifest in different forms, making them challenging to treat. Anxiety, agitation, and pain, in particular, are inextricably linked. Patients may become anxious because they anticipate pain, are experiencing pain, or remember pain that they have experienced [545,546]. Sedatives are often used in intensive care unit (ICU) patients to mitigate agitation and its consequences, such as self-extubation or self-harm [547]. Although first-line therapy for agitation and anxiety remains nonpharmacologic, at times administration of sedatives is needed for patient and staff safety.

1.1. *Balance of benefits and harms*

The administration of sedative agents may aid in the care of the agitated or anxious patient, but this must always be balanced against the deleterious effects of sedatives. Over-sedation can result in prolonged mechanical ventilation, increased incidence of pneumonia, hemodynamic instability, reduced mobility, withdrawal, delirium, and mortality [548]. These risks should be considered carefully as sedation has advantages, including reduction of anxiety/acute stress reaction/post-traumatic stress disorder, which allows for safe patient care. Appropriate sedation can accelerate patient recovery; inappropriate sedation can lead to complications and death.

1.2. *Values and preferences*

When and how sedation is administered is a function of the patient condition, the hospital environment, personnel expertise, and available resources. The number and types of sedative agents is often dictated by local drug availability and customs.

1.3. *Costs*

The monetary cost of sedative agents depends on drug availability, hospital contracts, and supply costs. Indirect costs include complications related to either over- or undersedation and include prolonged hospital stay, infection, and death.

Recommendation 2

Timely identification and treatment of the underlying causes of agitation are important prior to instituting sedative administration.

2. Considerations in formulating Recommendation 2

Underlying medical conditions can contribute to and/or be the source for agitation and anxiety [549]. The symptoms of agitation and anxiety include pain, delirium, hypoxemia, hypoglycemia, hypotension, or withdrawal from alcohol and other drugs. Treating these conditions with a sedative can result in adverse patient outcomes and even death. A careful search for a treatable disorder is important to ensure that agitation and anxiety are not due to a physical malady.

2.1. *Balance of benefits and harms*

Accurate diagnosis is essential in all aspects of medical care to assure optimal outcomes. Every drug, including sedative agents, has a distinct and described risk-benefit profile that should be considered for sedation episodes. The potential for harm exists in the misdiagnosis of a treatable medical disorder, over- or underdosing of sedatives, adverse drug interactions, and organ toxicity associated with sedative agents.

2.2. *Values and preferences*

Selection of sedative agents and route of administration will depend on local resources and customs. In resource-limited settings (RLS) the variety of sedative agents available may be restrictive or nonexistent. Individual practitioners and ICUs also develop preferences for sedative agents based on past experience, patient response, and drug administration/effects.

2.3. *Costs*

The direct costs of sedative agents will vary by country and hospital. Indirect costs related to administration include complications, inappropriate sedative use, and mortality. These costs are difficult to quantify but could contribute significantly to the cost of care. The use of sedation should be carefully considered and monitored.

Recommendation 3

Treatment of agitation and anxiety should begin with non-pharmacologic interventions when appropriate.

3. Considerations in formulating Recommendation 3

The use of sedative agents can often be either minimized or eliminated by identifying environmental or physiologic factors contributing to the agitation and anxiety. Nonpharmacologic interventions avoid the complications associated with sedative administration and often address the underlying cause of agitation. Such interventions include optimizing the environment, sleep provision (via appropriate hospital environment and routines), adequate analgesia, early mobilization, diversion therapy, and frequent reorientation. Use of

nonpharmacologic interventions is recommended for the ICU setting [549]. In RLS, pharmacologic sedation may be limited or unavailable in which case nonpharmacologic interventions may be the optimal strategy. Diversion, early mobilization, and frequent reorientation can effectively help reduce anxiety and agitation. Multiple methods for diversion, ranging from inexpensive ones (such as blowing bubbles to a 2-year-old) to complex expensive interventions (virtual reality machines) exist and have been reported to be effective. Additionally, because pain and agitation are linked, treatment of "pain first," in which interventions for pain are initiated prior to administration of sedatives, has become popular in the ICU setting [549]. Sleep deprivation, another important issue causing anxiety and agitation, is a frequent occurrence in ICU patients and may impair tissue repair, cellular immune function, and healing in addition to generating anxiety [550]. Provision of a hospital environment and routines conducive to sleep may avert or mitigate agitation.

3.1. *Balance of benefits and harms*

The use of nonpharmacologic interventions in the treatment of anxiety and agitation may afford a great benefit: avoidance of sedative use with its associated complications, potentially lower cost, universal availability, and adaptability to multiple different cultural environments. The risk of using nonpharmacologic interventions is that they may delay administration of effective sedation, mask physiologic injury, be costly, or not be regarded by the patient, staff, or family as a treatment.

3.2. *Values and preferences*

The nonpharmacologic technique chosen will depend on resource availability, staff knowledge, unit protocols, and patient experience. The effective application of nonpharmacologic techniques relies on knowledge of the norms and cultures in the burn care environment.

3.3. *Costs*

Nonpharmacologic techniques are readily available and in general incur a lower monetary cost than sedation administration. However, the effectiveness of these techniques depends on manpower, and skillful application which could be more costly in arenas with few health care providers.

Recommendation 4
When sedation is required, sedation scales and protocols should be used to monitor and adjust sedative administration to the lowest effective dose.

4. Considerations in formulating Recommendation 4

Sedation scales and protocols provide an objective measure for titration of sedative agents. These means have been shown to decrease the amount of sedation required, improve ICU patient outcomes (decreased duration of mechanical ventilation, ICU and hospital stay), reduce delirium, and impact long-term cognitive dysfunction [551–554]. Commonly used ICU sedation scales include the Richmond Agitation-Sedation Scale (RASS) and the Sedation-Agitation Scale (SAS) [549]. RASS and SAS have the highest psychometric scores for inter-rater reliability and discriminant validation, and have been tested in multiple patients. In addition, both scales showed moderate-to-high correlation with either electroencephalogram or bispectral index monitoring [555].

4.1. *Balance of benefits and harms*

Use of sedation scales provides an objective reference point against which to adjust medication administration. However, the effectiveness of scales depends on the presence of a protocol that adjusts sedation based on the scale score and on accurate use of the scale. Centers must have adequately trained staff and provide them with the knowledge base to conduct appropriate sedation testing. Inaccurate or incomplete testing may result in inappropriate medication administration.

4.2. *Values and preferences*

The type of scale and sedation protocol used will vary based on staff training, drug availability, and cultural norms. In RLS in which record-keeping and trained providers are limited, the application of a scale may pose institutional challenges.

4.3. *Costs*

The costs for monitoring sedation are primarily for manpower and documentation of scores. Personnel need to be trained on scale administration and appropriately recording scores. In addition, protocols that adjust medication administration based on sedation scores need to be developed.

Recommendation 5
When sedation is required, light sedation (patient arousable and able to purposefully follow simple commands) is preferred unless medically contraindicated.

5. Considerations in formulating Recommendation 5

Lighter sedation is associated with improved outcomes and patient ability to participate in therapy and activities. Deeper sedation may be necessary during times of critical illness when any movement may generate physiologic instability.

5.1. *Balance of benefits and harms*

In ICU adult patients, light levels of sedation are associated with shorter duration of mechanical ventilation and reduced ICU length of stay (LOS) [549]. Lighter sedation, however, can be difficult to attain and maintain. An undersedated patient may dislodge important medical devices, and an oversedated patient may develop complications related to immobility. Agent selection may be problematic, as patients may have variable responses to sedatives. Close monitoring and careful evaluation is essential.

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5.2. Values and preferences

The choice of agent, route of administration, and local drug availability will determine which sedative agents will be employed in any given setting. In general, the lowest dose of the most effective agent should be employed to achieve a light sedation level.

5.3. Costs

The costs of light sedation include drug acquisition and delivery costs, personnel costs related to administration and monitoring, and equipment costs.

Recommendation 6
Nonbenzodiazepine medications are preferred for sedation when resources permit.

6. Considerations in formulating Recommendation 6

Nonbenzodiazepine medications have been demonstrated to reduce duration of mechanical ventilation and ICU stay, shorten hospital LOS, reduce the incidence of delirium, and improve long-term cognitive function. Benzodiazepines have a variety of adverse effects, including respiratory depression, systemic hypotension (most pronounced when administered with a narcotic), and development of tolerance [556]. In addition, benzodiazepines are metabolized in the liver by the P450 enzyme system, and may accumulate with prolonged administration. This effect is exacerbated by renal failure, particularly with midazolam and diazepam, and clearance decreases with age [557].

6.1. Balance of benefits and harms

Each drug has a unique beneficial pharmacologic effect as well as untoward side effects. Practitioners should be familiar with the therapeutic and toxicity profiles of the nonbenzodiazepine medications available in their institution and carefully consider which agent would be most beneficial to the patient. The particular drugs available will be dictated by local resources and drug availability.

6.2. Values and preferences

The type of sedative agent used should be guided by the indications and sedation goals for the patient, the clinical pharmacology of the drug, availability, and the cost of the agent. Additional agents commonly used include propofol and dexmedetomidine. Propofol, which binds to multiple receptors in the central nervous system, has sedative, hypnotic, anxiolytic, amnestic, antiemetic, and anticonvulsant properties [549]. Unfortunately, propofol also causes a dose-dependent respiratory depression and hypotension from vasodilatation. Other adverse effects include cardiopulmonary instability, hypertriglyceridemia, acute pancreatitis, and myoclonus. Propofol infusion syndrome involves worsening metabolic acidosis, hypertriglyceridemia, hypotension, acute kidney injury, and arrhythmias. Dexmedetomidine, a selective alpha-2 receptor agonist, has a sedation pattern different from other sedative agents. It is analgesic/opioid sparing, and patients are more arousable and interactive, and have less respiratory depression [549]. However, dexmedetomidine may result in hypotension and bradycardia, particularly when intravenous loading doses are employed. Dexmedetomidine has been reported as safe for use in burns [558].

6.3. Costs

Options for sedation are dictated by local resources and contracts as well as staffing and drug side-effect profiles. The cost of the different sedative agents varies by region, hospital, and setting. In general, the least costly effective agent should be chosen for each patient.

Recommendation 7
Burn patients are at risk for and should be monitored for delirium.

7. Considerations in formulating Recommendation 7

Delirium, which impacts 80% of mechanically ventilated patients, is defined as an acute onset of cerebral dysfunction with either a change or fluctuation in baseline mental status, disorganized thinking, inattention, or altered level of consciousness [549,559]. As such, delirium signs include a disturbed level of consciousness with a reduction in ability to focus attention, and either a change in cognition (disorientation, language disturbance) or development of a perceptual disturbance (delusions, hallucinations). Sleep disturbance is common in delirium, as is fear, anxiety, anger, depression, and abnormal psychomotor activity. It is important to remember that delirium may be either hypoactive or hyperactive. Risk factors for delirium include pre-existing dementia, baseline hypertension, alcoholism, and high severity of illness on admission [549]. Delirium in burn patients is multifactorial and may be related to sedation, prior substance use, and disease-related factors. Delirium is associated with increased morbidity and mortality. Burn patients with moderate risk factors (receiving parenteral sedative and opioid medications; alcoholism history, cognitive impairment, sepsis, being on mechanical ventilation) should be monitored for delirium at least once per shift using an objective scale.

7.1. Balance of benefits and harms

Delirium is associated with multiple adverse outcomes, including increased mortality, prolonged ICU and hospital LOS, and development of post-ICU cognitive impairment. Once established, delirium is difficult to treat and is costly; prevention is essential. Hence, monitoring for delirium may improve overall patient outcomes and resource utilization.

7.2. Values and preferences

The specific methodology used to monitor and treat delirium is dependent on the resources available at a given burn

treatment setting. Nonpharmacologic therapies, such as ensuring sleep, increasing mobility, and providing frequent reorientation, may aid in the prevention of delirium development.

7.3. Costs

Delirium adds significantly to patient and institutional costs due to increases in hospital LOS, a need for additional medical treatment, and potential graft loss. An aggressive monitoring and prevention program for delirium can decrease both fiscal and patient costs.

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Blood transfusion

Note: Blood, for the purpose of these recommendations, is defined as packed red blood cells, as the vast majority of countries utilize packed red blood cells rather than whole blood for transfusions.

Recommendation 1

Blood transfusion is rarely indicated during burn resuscitation unless associated traumatic injury causing significant blood loss is present. During hospitalization blood should be transfused based on clinical assessment of the burn patient and families should be informed of the risks of transfusion.

1. Considerations in formulating Recommendation 1

To date, no optimal hemoglobin level has been defined for burn patients. Studies of intensive care units (ICUs) suggest that a hemoglobin measurement of 7 g/dL is safe for stable, young adult patients. Use of a lower transfusion trigger is supported across a wide variety of patient groups including those with pre-existing cardiovascular disease [560-578]. Retrospective studies of blood transfusions for major burns suggest a relationship between total units transfused in the ICU and mortality. A recently completed prospective multicenter randomized transfusion trial in burn patients found no difference of infection or mortality rates in transfusion targets between 7 g/dL and 10 g/dL [579]. Patients maintained at the lower hemoglobin value received fewer transfusions with no difference in wound healing.

Transfusion is rarely needed during resuscitation [580]. Thus, the commonly used burn resuscitation formulas do NOT include blood transfusion [581]. The traditional clinical signs that may support the administration of blood transfusion, including tachycardia, tachypnea, shortness of breath, fatigue, and weakness, are of limited utility, as these signs are ubiquitous in patients with >40% total body surface area burn (TBSA) [582,583].

1.1. Balance of benefits and harms

The administration of blood is beneficial but does carry significant risk. Adverse events include mismatching, transfusion reaction, Transfusion Related Acute Lung Injury (TRALI), Transfusion Associated Circulatory Overload (TACO), Transfusion Related Immunomodulation (TRAMI), electrolyte abnormalities, hypothermia, and transmission of infectious diseases [584]. These potential complications must be carefully weighed against the benefits of transfusion, which include amelioration of anemia, improved oxygen delivery, restoration of intravascular volume, decreased allograft rejection in transplant patients, and possible improvement in wound healing. There is evidence that the increased oxygen

delivery provided by blood transfusion may improve outcomes in patients with sepsis or acute coronary ischemia [585]. Families should be informed of the benefits and risks of transfusion prior to administration if possible.

1.2. Values and preferences

Blood availability and quality varies widely throughout the world. Hence, final transfusion practices will vary based on local resources. Likewise, cultural and religious preferences vary throughout the world and must be considered when making transfusion decisions.

1.3. Costs

Blood is a scarce and expensive resource that must be thoughtfully collected, stored, and administered. Costs for blood transfusion include product cost, personnel costs, equipment costs (specialized intravenous tubing is required for transfusion), storage costs, and opportunity costs (blood used for one patient may limit a center's ability to transfuse another individual). A restrictive transfusion policy decreases overall transfusion costs.

Recommendation 2

Blood transfusions should be administered one unit at a time unless the patient is hemodynamically unstable or actively bleeding. Patients should be reassessed prior to the administration of a second unit of blood.

2. Considerations in formulating Recommendation 2

Blood bank organizations recommend that blood be transfused one unit at a time to avoid the complications associated with transfusion [586]. Studies examining the timing of hemoglobin monitoring after transfusion have demonstrated that in the stable nonbleeding patient, hemoglobin levels drawn as early as 15 min after transfusion will demonstrate the effects of the transfusion on hemoglobin levels [587,588]. Transfusing one unit at a time also reduces the incidence of TACO. Operative transfusions should be carefully considered and administered in response to significant bleeding

2.1. Balance of benefits and harms

The risks associated with transfusion of blood increase with the number of units transfused. The more units transfused, the greater the likelihood that the patient will develop antibodies, have a transfusion reaction, or develop TACO or TRALI. Actively bleeding patients or those who are hemodynamically unstable due to ongoing cardiac ischemia or sepsis may benefit from multiple units of blood. However, the routine transfusion of multiple units is discouraged.

2.2. Values and preferences

The threshold for blood transfusion during times of active bleeding will vary by situation, location in the hospital, resource availability, and resource quality. For example, in some settings, blood may not be readily available for transfusion, which may alter decision-making. Different providers also set varying thresholds when using blood as a volume expander during periods of sepsis.

2.3. Costs

Administering units of blood one at a time decreases overall hospital costs in several ways. First, fewer units of blood will be transfused. Second, because fewer units of blood are transfused, the likelihood of transfusion reactions and complications will be reduced. The cost of the single unit transfusion strategy lies in the resources required to measure a hemoglobin level between transfusions.

Recommendation 3

Blood type should be confirmed and blood should be cross-matched prior to transfusion unless an emergent need (such as massive hemorrhage) is present.

3. Considerations in formulating Recommendation 3

Each hospital should establish a system for blood transfusion administration that follows the international standards set by the World Health Organization (WHO) [589]. Clerical errors and instances of mismatched blood remain common. A two-specimen requirement has been instituted to reduce the incidence of type and cross error [590]. Blood type and cross-match should also preferably be confirmed by two providers prior to administration, and patients should be monitored during transfusion.

3.1. Balance of benefits and harms

Recommendation 3 is designed to improve the safety of blood transfusion across all settings, as mismatched blood transfusion can incur a potentially lethal reaction. However, in exsanguinating hemorrhage, as can occur in major surgical excisions, the patient can be harmed if denied a life-saving transfusion. In some settings blood must be obtained from another institution; hence, the availability of type-specific blood may be limited.

3.2. Values and preferences

Providers will use different thresholds in defining "emergent need" for blood transfusion based on resource availability, personal experience, and patient/family religious and cultural preferences. In addition, different settings may have different blood cross matching capabilities, which may result in delayed or inaccurate cross matching.

3.3. Costs

Cross matching of blood is an additional cost for the institution and potentially for the patient. The cost of a transfusion reaction, however, may supersede these costs.

Recommendation 4
Blood tests should be restricted to those necessary for patient care, and the amount of blood used for testing should be minimized to reduce the need for transfusion.

4. Considerations in formulating Recommendation 4

Multiple studies have demonstrated that frequent blood testing in critically ill patients can result in significant blood loss and even the need for transfusion [591–593]. Blood transfusion has been associated with multiple complications including infection, TRALI, TACO, hemolytic reactions, nonhemolytic febrile reactions, allergic reactions, air embolism, hyperkalemia, citrate toxicity, hypothermia, and coagulation abnormalities [584]. Reducing the volume of blood drawn and decreasing the frequency of testing will reduce the amount of blood needed.

4.1. *Balance of benefits and harms*

Although frequent blood sampling may result in anemia and the need for transfusion, frequent testing during times of patient instability may be needed to rectify ongoing physiologic perturbations. Blood sampling should be thoughtfully considered and discontinued when patient stability permits.

4.2. *Values and preferences*

Provider experience, laboratory capabilities, resources available to obtain blood samples, and patient status all influence the decision to obtain blood tests. Some centers may not have the capability of analyzing small volume samples.

4.3. *Costs*

Blood sampling has both testing and patient costs. The cost of testing and the supplies required for testing may be a limiting factor in resource constrained settings. In addition, frequent blood sampling may increase the need for further transfusion and testing. Hence, clinicians should carefully consider immediate and delayed costs associated with transfusion.

Recommendation 5
The use of erythropoietin to reduce transfusion requirements after burn injury has not been validated in burn patients.

5. Considerations in formulating Recommendation 5

Critically ill patients frequently require blood transfusion: 85% of critically ill patients who remain in an ICU for greater than 1 week require blood transfusion, largely attributable to a blunted erythropoietic response [594]. In a prospective randomized trial in an ICU (not including burn patients), patients receiving erythropoietin required fewer blood transfusions [595]. A single-center study of erythropoietin in burn patients did not confirm these findings, but an animal study suggested decreased burn progression after the use of erythropoietin [596,597]. Further study is needed to confirm or refute these findings.

5.1. *Balance of benefits and harms*

Although erythropoietin may have utility in critically ill burn patients, evidence supporting its routine use is lacking. In addition, erythropoietin side effects may include thromboembolism, iron deficiency, and arterial hypertension.

5.2. *Values and preferences*

Recombinant human erythropoietin may not be available in a resource-limited setting (RLS). In patients who refuse transfusions due to religious, personal, or cultural beliefs, erythropoietin may be a viable alternative to reduce the need for blood transfusion.

5.3. *Costs*

Recombinant human erythropoietin is an expensive drug that may be limited in availability in many settings. Studies comparing erythropoietin to iron to ameliorate the effects of anemia in surgical patients are mixed [598].

Recommendation 6
Blood substitutes have not been validated for use in burns and should not be used after burn injury except as a life-saving effort in patients refusing blood transfusion.

6. Considerations in formulating Recommendation 6

The use of blood products to improve oxygen carrying capacity is unparalleled by any current blood substitutes. Hemoglobin-based oxygen carriers have not been tested in burn patients and therefore cannot be recommended for routine care. Some existing case reports detail the use in burn patients of hemoglobin-based oxygen carriers combined with intravenous iron therapy, but insufficient evidence supports a recommendation for their routine use [599,600].

6.1. *Balance of benefits and harms*

Patients with major burns may develop significant anemia due to decreased red blood cell generation, increased red blood cell destruction, and blood loss due to surgery or phlebotomy. The use of blood transfusion may be restricted due to lack of blood availability or patient preferences. Hence, the use of blood substitutes as a volume expander may need to be considered as a life-saving alternative in patients with severe anemia who cannot or will not consent to blood transfusion.

6.2. *Values and preferences*

Citing cultural, religious, or personal beliefs, some patients may refuse blood transfusion. Blood substitutes may be used by some providers in an attempt to restore oxygen delivery in severe anemia.

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6.3. Costs

Blood substitutes are not readily available and incur costs related to product, processing, delivery, and monitoring of the patient.

Recommendation 7
During massive surgical blood loss, consideration should be given to administering plasma and platelets in a 1:1 ratio if resources permit.

7. Considerations in formulating Recommendation 7

Burn excision and grafting can cause life-threatening bleeding, particularly when excision is delayed or during massive excision. Blood loss from burn excision in children approximates 2 mL/% burn excised for all areas except the head, where blood loss is approximately 5 mL/% burn excised; and in adults estimates have approached 10 mL/% burn excised [601,602]. Hence, strategies to reduce transfusion have been developed (as described in the ISBI Practice Guideline for Surgical Management of the Burn Wound) [603]. A recent multicenter trial of the use of a 1:1:1 blood transfusion:plasma transfusion:platelet transfusion in traumatic massive blood loss demonstrated improved survival compared to less aggressive approaches [604]. A prospective trial of a 1:1 vs. 4:1 PRBC:FFP ratio in children demonstrated a decrease in number of units of blood transfused, but no improvement in outcomes [605].

7.1. Balance of benefits and harms

All blood products carry inherent risks, including fresh frozen plasma, platelets, and red blood. Utilization of an aggressive policy for product transfusion must be carefully weighed against the potential complications of the products to be transfused. The benefit of a 1:1:1 transfusion strategy has been demonstrated in cases of massive blood loss; hence, use of the 1:1:1 policy should be restricted to that setting pending further studies supporting this practice in burns.

7.2. Values and preferences

Different providers will use different thresholds for defining "massive" transfusion in burn patients due to local practices, blood product availability, and blood product safety. Likewise, the setting in which a massive transfusion protocol is administered will vary based on local resources and expertise.

7.3. Costs

Use of a massive transfusion protocol will be restricted due to the cost and availability of blood products, the safety of the available blood products, and the opportunity cost of administering and monitoring the effects of blood products.

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Deep venous thrombosis

Recommendation 1

Due to the risk of deep venous thrombosis (DVT) after burn injury, adult burn patients should be evaluated for DVT risk, and those with moderate-to-high risk should receive chemoprophylaxis unless a medical contraindication exists.

1. Considerations in formulating Recommendation 1

Reports from the scientific literature cite the risk of burn patients developing DVT as ranging from 0.25% to 1.77% in symptomatic patients. In studies where routine screening was employed, the incidence was much higher, ranging from 5.92% [606] to 53% [607]. A recent prospective study reported an 8% incidence of DVT in young adult burn patients with burns >40% total burn surface area (TBSA) who had not received any

chemoprophylaxis [608]. The risk estimation for DVT in children with burns has not been reported.
The clinical diagnosis of DVT based on the history and physical examination may be erroneous, as 50% of the cases are asymptomatic. Additionally, in patients with lower limb burns the clinical signs and symptoms of DVT may be attributed to the edema associated with injury [609].
Prospective screening of the deep veins of the extremities by Doppler imaging can lead to very early detection of DVT in burn patients, and patients with DVT can benefit from early therapy [608]. D-dimer estimation provides limited value in screening burn patients for development of DVT because of extremely low specificity and low positive predictive value [608]. It has been suggested [610] that risk estimation in burn patients can be made using weighted scores for risks assigned to burn size and inhalation injury [611], and including these scores in the Caprini scale [612].

1.1. *Balance of benefits and harms*

In a retrospective study of 4102 patients, Fecher et al. reported no complications using routine chemoprophylaxis with heparin [613]. Bushwitz et al. found no incidence of heparin-induced thrombocytopenia in their retrospective study of 1111 burn patients (600 patients with heparin prophylaxis and 511 patients with enoxaparin) [614].
There have been reports of bleeding in 4% patients with the routine use of chemoprophylaxis [615], and of heparin-induced thrombocytopenia and formation of antiplatelet antibodies in 1–5% of patients [615,616]. As a result, chemoprophylaxis has not been universally adopted for DVT prevention in burn patients. However, development of these complications was significantly less if low molecular weight heparin (LMWH) was used in prophylaxis [616].
The 30% incidence of postphlebitic syndrome in burn patients and the potential mortality from pulmonary embolism (PE) may warrant routine chemoprophylaxis [613,617,618]. Since the first manifestation of the disease may be a fatal PE it may be inadvisable to treat only after symptoms are manifested [618].
In the absence of prospective studies, it was suggested that because the incidence of DVT is high in burn patients, routine prophylaxis is warranted [619]. However, since the efficacy and complications of prophylaxis remain undocumented, selective use of chemoprophylaxis in high-risk groups is recommended although the definition of a high-risk burn group remains undefined [619].
The incidence of developing DVT on chemoprophylaxis is between 0% [610] and 0.27% (Bushwitz et al.) [614]. The extremely low risk of complications reported in the latter solitary prospective study, along with zero incidence of developing DVT in burn patients on chemoprophylaxis [610] argue for the current recommendation for patients to be evaluated via calculation of weighted risk scores, as mentioned above.

1.2. *Values and preferences*

There is no current consensus on the use of chemoprophylaxis in burn patients [620,621]. A survey study of 84 United States burn centers found 76% of the centers provided routine DVT prophylaxis whereas 24% of the centers did not provide any form of prophylaxis [620]. Another survey of 16 Canadian burn centers found 50% of the centers using routine prophylaxis and 25% using it only for the high-risk groups [621]. The remaining 25% did not use any form of prophylaxis.

1.3. *Costs*

Cost of prophylaxis can be a concern in some countries as LMWH can be expensive. Still, the direct costs of chemoprophylaxis in burn patients have never been calculated. However, if used judiciously in the high-risk group, as defined above, prophylaxis can be beneficial in curtailing or eliminating the incidence of DVT or PE in the burn population.

1.4. *FAQs*

Q. Should antifactor Xa activity be monitored with LMWH?
A. Few studies with burn patients have investigated the use of LMWH to monitor antifactor Xa activity. One study based on the measurement of antifactor Xa suggested that LMWH is commonly underdosed in burn patients [622]. However, a recently published systematic review in obese patients categorically stated that routinely determining concentrations of anti Xa activity to monitor the clinical efficacy of LMWH was not warranted. Anti Xa activity could be predicted from the dose of LMWH and body weight. Monitoring anti Xa activity may help in clinical decision-making only when there is an unexpected clinical response and the elimination of LMWH is impaired [623].
Q. What is the appropriate dose for LMWH in DVT prophylaxis?
A. Enoxaparin dosage for prophylaxis of DVT has been variously prescribed as 40 mg subcutaneously once a day for abdominal surgery to 30 mg every 12 h for joint replacement surgery [624]. There is no such recommendation for burn patients. However, in the only randomized controlled trial available on this topic the authors used 30 mg twice a day and reported no DVT in the study group [610].
Q. Is there any advantage in using fondaparinux over LMWH or unfractionated heparin?
A. Fondaparinux is a synthetic inhibitor of factor Xa which is chemically related to LMWH. The only advantage of using fondaparinux over LMWH or unfractionated heparin is that the risk of developing heparin-induced thrombocytopenia is much lower [625].

Recommendation 2
Effective DVT prophylaxis in burn patients can be rendered using pharmacologic low molecular weight heparin and/or physical strategies.

2. Considerations in formulating Recommendation 2

Every burn center should develop a formal strategy for prevention of DVT [626]. Mechanical prophylaxis methods do reduce the risk of DVT, although they have not been studied as intensively as pharmacologic options [627]. Mechanical prophylaxis can be provided by elastic compression stockings,

foot impulse devices or intermittent compression devices. A meta-analysis confirmed that intermittent pneumatic compression can substantially diminish the risk of developing DVT, but it may not prevent the development of PE [628]. For the high-risk patient groups it is recommended that a combination prophylaxis regimen be adopted (intermittent pneumatic compression with chemoprophylaxis) as this is associated with significantly lower venous thromboembolism (VTE) risk [629,630]. Mechanical prophylaxis may be the primary modality of prophylaxis in patients who are at a high risk of bleeding [626]. Mechanical devices and stockings may not be applicable if lower extremities are burned.

2.1. *Balance of benefits and harms*

Elastic compression stockings have been shown to effectively reduce symptomatic DVT; however, their use is also associated with an increase in skin-related complications. The reasons for noncompliance with graduated elastic stockings include pain, discomfort, difficulty donning the stockings, perceived ineffectiveness, excessive heat, skin irritation, cost, and appearance [631–633]. Accessibility of these devices may be limited in resource-limited settings.

2.2. *Values and preferences*

Patient compliance and the appropriateness of the site of compression are the prime factors in determining the type of mechanical prophylaxis to be used [634]. Compression stockings function more by preventing stasis and distention of veins. Elastic compression stockings have traditionally been recommended as an important adjunct to pharmacologic treatment in patients with DVT, particularly for the prevention of postthrombotic syndrome (PTS). However, the latest American College of Chest Physicians guidelines do not support their routine use [635]. A randomized, placebo-controlled study suggested that stockings did not help prevent PTS [636], although this conclusion is controversial. The evidence for the prophylactic effect of the stockings to prevent DVT in medically ill patients is at best low to moderate [637]. Graduated compression stockings are more acceptable and have better compliance than non-elastic bandaging or pneumatic devices [638].
No evidence supports an improvement in DVT prophylaxis for pneumatic compression devices via rapid inflation, high pressures, or graded sequential intermittent compression systems [634]. Currently, there is little evidence to formulate recommendations for a specific device or type of device for DVT prophylaxis [639].

2.3. *Costs*

The cost-effectiveness of thromboprophylaxis is robust in many medical and surgical patients, but no cost model has been developed for trauma patients [639]. Use of mechanical prophylaxis can also be expensive. The extent of benefit with combined chemoprophylaxis and mechanical prophylaxis has not been studied in the burn population.

2.4. *FAQs*

Q. For how long should mechanical prophylaxis or chemoprophylaxis be continued?
A. DVT prophylaxis should be continued until the patient has regained sufficient mobility.

Recommendation 3
Early mobility increases patient strength and may influence the risk of DVT development.

3. Considerations in formulating Recommendation 3

Contraction of muscles is an important factor in helping to keep blood flowing through the veins, particularly in the legs [640]. Prolonged immobility in trauma and critically ill patients has been repeatedly stressed as a well-known risk factor for developing DVT [640,641] and thus provides the rationale for the recommendation that DVT prophylaxis be discontinued only if the patient gains sufficient mobility.
A recently published study [610] confirmed that prolonged immobility in burn patients is a significant factor in their developing DVT ($p < 0.001$), even if some previous studies could not establish this strong link in burn patients [617,618,642].
Prolonged immobility in burn patients can result from their having sustained extensive burns or burns of the lower extremities, or from inhalation injury or critical illness. Femoral catheters or intravenous cannulae in lower extremities can also contribute to immobility. Generally speaking, burn patients who have a prolonged hospital stay are more critically ill and hence more prone to developing DVT [617,642]. Early ambulation should translate to early discharge from the hospital [610]. The presence of lower limb burns has been reported as a risk factor in several studies [617,642].

3.1. *Balance of benefits and harms*

Minimal evidence supports that immobility improves patient outcomes, with the exception of cases of major hemodynamic or respiratory instability, in which patient movement can precipitate acute decompensation.

3.2. *Values and preferences*

No reports document immobility as a preference. Surgeons may prefer maintaining their patients at bed rest after major excision and grafting to avoid graft shearing and loss, especially when it involves the lower limbs. However, the duration and efficacy of this approach has been questioned.

3.3. *Costs*

Early mobility will definitely reduce the cost of mechanical or chemoprophylaxis by reducing its necessity. However, increased resources (personnel, equipment) to initiate mobility may restrict its applicability in some environments.

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Psychiatric disorders

Recommendation 1

Patients should ideally be screened for psychiatric and social risk factors that impact safety and well-being. The following screenings should be performed:

1. ***Upon admission: Mechanism of injury (self-inflicted or abuse/neglect), social support resources, housing and food resources, blood alcohol level;***
2. ***During inpatient hospitalization: Depression, acute stress disorder (ASD)/post-traumatic stress disorder (PTSD), anxiety, substance use disorder; and***
3. ***Within the first month of hospital discharge, then as needed thereafter: Depression, ASD/PTSD, anxiety, substance use disorder.***

1. Considerations in formulating Recommendation 1

These recommendations were formulated based on the biopsychosocial model of burn recovery, which emphasizes the relationship between premorbid risk factors, injury-related variables, and interpersonal variables on both short- and long-term outcomes [643]. After completion of the resuscitation phase, psychological and social aspects of recovery should be addressed in conjunction with aspects of physical recovery. The burn center is in a critical position to intervene in promoting behavior change and alleviating social ills, particularly if high-risk behaviors or lack of social resources (e.g., food and shelter) have led to the injury. These high-risk behaviors and circumstances can also put patients at risk for future injury and may inhibit recovery if they are not addressed [644].

Social risk factors include lack of food and shelter, lack of social support, and when the burn injury was sustained as a result of domestic violence or assault. These social risk factors should be assessed on admission to facilitate early intervention and identify potential resources during hospitalization.

Psychiatric issues can be categorized in two ways: (1) those that are premorbid and which potentially contributed to the burn injury and (2) those that develop as a result of the burn injury itself. Despite the origin, psychiatric issues are risk factors for future injury and can impede recovery and decrease long-term quality of life.

The most common psychiatric issues contributing to the burn injury include self-immolation and substance use. Intentional self-inflicted burn injuries, such as self-immolation, are rare in the United States, Europe and Australia, typically accounting for about 1–6% of burn unit admissions [645]. However, self-inflicted burn injuries account for up to 25–30% of burn unit admissions in poorer regions of the world. Intentional self-inflicted burn injuries are often associated with larger total burn surface area (TBSA), inhalation injury, longer hospital stays, and increased mortality. If patients do survive their burn, they will need more intensive outpatient follow-up to treat the issues that led to the suicide attempt [645].

Alcohol use disorders are endemic among trauma patients, and a body of literature supports the effectiveness of alcohol screening and brief interventions in the trauma setting. As a result, several countries have mandated that specialty trauma centers screen for alcohol use disorders and have a mechanism in place for a brief intervention. Furthermore, trauma center providers from various disciplines can be trained to deliver highly effective screening and brief interventions [644].

International guidelines, such as the Standards and Strategies for Burn Care [646] and the guidelines of the American Burn Association (ABA) quality improvement consensus committee, [647] recommend screening for depression and ASD/PTSD following a traumatic injury, as they are the most common disorders that can impact healing. We also recommend anxiety screening (as discussed in the Sedation guideline, see p. xx), as anxiety is linked with pain and is common in patients with burn injuries at all phases of recovery. Long-term quality of life is impacted by burn severity as well as the presence of post-burn depression and post-traumatic stress symptoms. Both have been associated with poorer physical and social function, poorer quality of life and interference with the return to work [648,649].

Prevalence rates for depression following burn injury vary according to the assessment measure being used and the time frame of administration, ranging from about 10% at discharge to 20–30% at one year after injury [650]. It is important to treat depressive symptoms even if the patient does not meet criteria for a DSM-V (Diagnostic and Statistical Manual of Mental Disorders, 5th edition) diagnosis as symptoms can interfere with care and impact motivation for intensive burn treatment [651].

As with depression, prevalence rates of ASD vary depending upon assessment measure and time frame but generally range from 6% to 33%. PTSD is more common, with rates of 24–40% at 6 months post injury, and the rate at one year after injury is around 50% [652]. The presence of ASD in the acute care setting can often mimic delirium and/or increase agitation, leading to overuse of sedation and pain medication. Further, the ongoing painful nature of burn care can also be considered a recurrent trauma, with patients having ASD symptoms related to burn care and not the initial injury. Some studies have linked the presence of post-traumatic stress symptoms to increased pain and reduced wound healing through the presence of oxytocin and pro-inflammatory cytokines [653]. Early intervention of ASD symptoms can actually mitigate the onset of PTSD, thus supporting the argument for early screening and intervention. As with depression, a person should be treated even though they do not meet criteria for an actual diagnosis [647].

Virtually all patients with a lengthy hospitalization for a burn injury experience anxiety; however, anxiety can be hard to detect and often manifests as pain. Anticipatory anxiety, anxiety prior to a procedure such as a dressing change, is also common. Furthermore, anxiety is complicated by delirium and increased agitation. It is unlikely that a patient will meet full

DSM-V criteria for a diagnosis of generalized anxiety disorder (GAD), and screening tools for GAD in the inpatient setting are not likely to be useful. However, as discussed in the guideline on Sedation, detection of anxiety can be made using behavioral indicators, such as poor sleep, agitation, fear of painful procedures or increased pain reports prior to a procedure. Anxiety should be treated using nonpharmacologic methods first, followed by pharmacologic approaches. Several disciplines represented on the burn team, such as nursing and occupational therapy/physical therapy and social work now undergo nonpharmacologic anxiety management as part of their training and these interventions should be utilized.

It is important to note that the presence of delirium can invalidate screening for specific disorders. Since delirium can wax and wane, the timing of screening can be complicated, necessitating repeat screenings. At a minimum, patients will need to be screened during times of lucidity, and a brief assessment of delirium should accompany screening for ASD, anxiety and depression. In general, patients should be screened at least once while in intensive care, at least once during acute care or rehabilitation, and at least once in the outpatient clinic. If the initial screen is negative, patients should continue to be screened at various points throughout the hospitalization.

Although several studies have sought to identify risk factors for PTSD [652] and depression [654], no reliable set of patient characteristics can accurately predict who will develop this disorder; therefore, every patient admitted to the burn center or assessed in the outpatient burn clinic should be screened. Further, injury severity does not seem to be an accurate predictor so even those with smaller burns should be screened. The screening tools selected should be brief and easy to use by any provider.

1.1. *Balance of benefits and harms*

According to the evidence, early screening and intervention for these disorders leads to better outcomes. Potential harms include screenings that uncover psychiatric issues needing intervention and not having a plan in place for mental health providers to provide that intervention. A burn center team may be more at risk for liability if it screens for a disorder and then ignores a positive screen.

1.2. *Values and preferences*

Although there are screening tools available for both adults and children for the various psychiatric issues mentioned, none of them are specifically validated for the burn population. Therefore, each burn center should select the screening tool most appropriate for its population, taking into account language and cultural aspects of the tool. Many general quality-of-life screening tools will not be sensitive or valid in the inpatient setting. It is important to pick short screening tools that are specific to the symptoms that you want to detect (e.g., PTSD, depression, anxiety).

Screening for delirium and pain are critical during the inpatient phase of hospitalization as these conditions can affect all aspects of recovery See also guidelines for Sedation, p. xx and Pain Control, p. xx.

1.3. *Costs*

Cost of screenings will vary by country and according to the measure used. Many free screening measures are available for public use. The costs of untreated mental health and substance use disorders that put patients at risk for further injury is well documented [655]. For example, widespread screening and brief interventions for substance use disorders can result in substantial health care cost savings by cutting down on repeat emergency department and primary care visits. In some countries, screening for psychological disorders will be required for full insurance reimbursement [647].

1.4. *FAQs*

Q. What is the difference between ASD and PTSD?

A. Although there are subtle differences, the defining characteristic is time frame. ASD is diagnosed from day 3 to 30 following a trauma and PTSD is the diagnosis after day 30. Full diagnostic criteria for both disorders can be found in the DSM-V Manual [651].

Q. If patients present with a positive bronchoalveolar lavage (BAL), should they be treated for alcohol withdrawal?

A. A positive BAL does not necessarily indicate chronic alcohol abuse. However, alcohol withdrawal can be a life-threatening condition, and if a burn patient is suspected to be at risk of developing alcohol withdrawal symptoms, burn care providers should follow their own hospital protocol.

Recommendation 2

Patients who screen positive for psychiatric disorders should be offered treatment within a burn center, via a hospital consultation/liaison service, or by a community outpatient provider. At minimum, burn centers need access to a psychology/psychiatry hospital consultation service for their inpatients and a list of mental health providers in the community.

2. Considerations in formulating Recommendation 2

Screening and treating psychiatric symptoms requires a plan and resources in place to treat patients with symptoms. Ideally, a mental health provider (psychiatrist, psychologist or social worker) will be part of the multidisciplinary burn center team. However, at the very least every center should have resources available to ensure appropriate referral to mental health services to further assess difficulties and intervene appropriately.

In the general trauma population, evidence documents that a stepped model of care improves outcomes such that patients exhibit significantly better mental health at 12 months post injury [656]. This stepped model includes inpatient screening for PTSD, anxiety, and depression; and 4–10 sessions of cognitive behavior therapy for those who screen positive. Early inpatient screening for these disorders identified 89% of those who went on to develop anxiety or an affective disorder at 12 months.

Brief interventions for ASD/PTSD, depression, and anxiety should be initiated in the inpatient setting for anyone who

screens positive for these disorders. However, it may be easier to receive more intensive treatment in the outpatient setting once survival is more certain, pain is better managed, and mental status has improved. A survey of burn survivors found that when outpatient clinics were conducted exclusively by medical doctors with no supportive multidisciplinary team, patients were dissatisfied with care [657,658].

In resource-limited settings (RLS), mental health providers who have experience specifically treating patients with burn injuries may not be available. It is perfectly acceptable to refer to a mental health professional who has experience providing evidence-based treatment for PTSD, depression and anxiety. Several evidence-based treatments for PTSD, depression and anxiety exist; however, discussion of these treatments is beyond the scope of these guidelines. In addition, treatments are validated based on relevance in the language and culture in which they are performed and a treatment that is validated in English-speaking Americans, for instance, may not be valid in other languages or parts of the world. Mental health providers are licensed and boarded in the state or region in which they practice and it is up to those licensing boards to ensure that the providers are knowledgeable of culturally relevant treatments for their region.

2.1. *Balance of benefits and harms*

Referring a patient with a positive screen for further assessment and treatment from a mental health professional incurs little harm. Cultural norms may restrict the follow-through on recommendations for further mental health care. Hence, caution must be used to present the issues to the patient and family in the context of the culture involved. The potential benefits of psychiatric intervention are great in that treatment will likely improve quality of life and enhance the physical recovery from the burn injury.

2.2. *Values and preferences*

Each culture has unique perspectives on psychiatric illness and its treatment, which may either enhance or impede patient and family acceptance of therapeutic intervention. Likewise, in RLS, funding for mental health follow-up may be limited. In these cases the burn center should acknowledge the regional deficit and develop strategies to assist patients with mental health needs.

2.3. *Costs*

The costs of not providing access to treatment can be great for both the patient and society [659]. Rarely do psychiatric symptoms improve without treatment, particularly if they have been consistently present throughout burn treatment.

2.4. *FAQs*

Q. If we do not have the appropriate resources in place to provide referrals for interventions, should we forego screening entirely?

A. You may want to conserve your resources and eliminate standard screening tools, but most bedside nurses and burn therapists will recognize behavioral symptoms of distress in the course of their treatment and many have been trained to alleviate distress. In the outpatient setting, it might be useful to find online resources that address many symptoms of distress in burn survivors. For example, both the Phoenix Society (https://www.phoenix-society.org) and the National Institute on Disability, Independent Living, and Rehabilitation Research (*NIDILRR*) burn injury model systems (https://msktc.org/burn/factsheets) have online resources for both patients and burn care providers. Many of these fact sheets and materials are available in both English and Spanish.

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Outpatient burn care

Recommendation 1

Burn centers should provide outpatient care for smaller burn injuries and for follow-up of patients with larger burns after completing their hospital treatment.

1. Considerations in formulating Recommendation 1

Outpatient care should be integrated into the burn-center service region either by health professionals seeing the patients directly or, in select instances, by supporting other care providers (general practice settings) in the community through an outreach program. Partial thickness burns of <10% total body surface area (TBSA) in children and 20% TBSA in adults could, in certain circumstances, be cared for in the community by liaisons with a burn center. However, in resource-limited settings (RLS), with scarce transportation, local adaptations are important.

In 2004, the World Health Organization (WHO) estimated that 11 million people worldwide were burned severely enough to require medical attention [660]. The vast majority of patients can be safely treated in an outpatient setting with a good outcome. Unfortunately, most burn epidemiology research only examines inpatients with little data available on the scale and quality of outpatient care. In developed parts of the world, it is estimated that at least 90% of patients are treated in the community [661], and only 1% of patients seen at emergency departments have a burn injury [662]. Little is known of outpatient care provided to burn patients in both developed countries and RLS.

The burn size-thresholds above which burn patients require hospital admission are widely described in referral guidance proposed by a number of national and regional burn societies [663–665]. These guidelines describe in detail the complexity of burn injuries that necessitate specialized burn expertise. Understandably, these criteria differ in different regions of the world. The International Society for Burn Injuries (ISBI) practice guidelines group recognizes these challenges, especially where resources are limited and safe transportation can be scarce. Noncomplex partial thickness burns <10% TBSA in children and <20% in adults could be safely cared for in the community in liaison with a burn center. However, all burns that are unlikely to heal within 2 weeks should be considered for referral to a burn center. It must be emphasized that local adaptations are important and local policy should take into consideration the available resources. Burn patients treated post discharge by burn centers in a hospital are best cared for either in an outpatient setting directly by the burn center team or with their guidance by other health professionals outside the burn center.

Outpatient burn care, when integrated with burn centers, achieves optimal care for minor burns that do not require hospital admission, and also smooths the transition for patients with larger and complex burns after hospital discharge, when they are most vulnerable. Fully integrated outpatient care within the burn center ensures quality and continuity of care, reduces length of hospital stay, improves the inpatient center capacity, reduces costs by reducing the total number of registered nurses [666], and allows flexibility in resources. More importantly, outpatient care integrated with burn centers ensures a high standard of adherence to infection control policies, as patients are managed by burn-experienced staff [667]. Outpatient burn care follow-up allows the opportunity for ongoing management of burn sequelae that may affect a patient's quality of life after sustaining burn injury (pain, itch, contracture, etc.) [668].

1.1. *Balance of benefits and harms*

Strong evidence documents the importance and value of providing outpatient care for burn patients. The benefits are compelling and outweigh the potential risk of travel and additional costs for either the patients or the health professionals who manage satellite clinics. Lack of outpatient care may prove harmful to patients, with the potential for complications to go unnoticed and the risk of serious, or in some cases, lethal consequences.

1.2. *Values and preferences*

Providing outpatient burn care is an essential part of a medical service and this can be challenging in RLS. Transportation to the burn center may not be available and patients with larger burns may stay in the community. Other social or family circumstances can also be an obstacle; burn center support, either through telemedicine or mobile communications may help these vulnerable patients.

1.3. *Costs*

An integrated outpatient service within the burn center incurs an additional cost. However, this cost could be offset by decreasing the length of hospital stay, reducing the number of hospital readmissions, and lowering after hospital discharge the incidence of complications, such as wound breakdown and infection. Furthermore, flexible cooperation between the inpatient and the outpatient staff can reduce personnel costs.

Recommendation 2

Burn centers should establish multidisciplinary burn care outreach programs to support providers where travel is difficult in their region.

2. Considerations in formulating Recommendation 2

Centralizing burn care with the establishment of burn centers has certainly improved treatment outcomes [669–671]. Essential to the success of burn centers is the definition of clear care-pathways, the implementation of quality improvement and training programs, and the dissemination of good practice guidelines and education to other providers in their region who do normally manage minor burns.

A study from the Burns Registry of Australia and New Zealand showed that outpatient workload is 2.2:1 when compared to inpatients [672]. However, only 10% of patients with burns seen in a hospital setting are admitted to a hospital [661]. Data from the British burn database are similar [673]. As the vast majority are treated in the community, it is imperative that burn centers set up a program to care for these patients, either directly by establishing satellite clinics, staffed by the burn center multidisciplinary team, or indirectly by training local practitioners on the management of minor and, in certain circumstances, moderate burns. The latter option is more efficient and cost-effective.

Telemedicine has been shown to be technically and clinically feasible [674,675], safe, and cost-effective [676]. In particular, telemedicine has a considerable benefit on patient triage to burn centers and helps to avoid wasting valuable transportation resources with unnecessary transfers [677]. Furthermore, clinical reviews and advice to primary and secondary care providers could be readily established by holding regular virtual outpatient clinics where patients are reviewed and wounds examined in a multidisciplinary setting.

Burn center outreach programs may also include training and education for all other burn care providers in their region. Mobile communications are now available in most urban and rural communities across the globe and can be used as a fast communication channel throughout a region, especially during emergencies. Regular face-to-face workshops and webinars are also valuable tools to disseminate good practice guidelines and discuss care pathways within the region. The outreach program should also include education for the general public as part of a burn prevention program. This is now more feasible using social as well as regular media in public awareness campaigns.

2.1. *Balance of benefits and harms*

Significant evidence in the literature supports the concept of outreach burn care. Outreach programs are important for the provision of direct patient care including wound care, physical therapy and psychological rehabilitation. This ensures that care is provided efficiently nearer to where patients live, reducing costs and avoiding wasted resources required for transportation. Nonetheless, if the outreach service is not adequately managed, patients may be denied standard of care treatment. As outreach team members sometimes work independently from the rest of the multidisciplinary team, rigorous documentation and regular auditing is required to safeguard against any deviations that may occur from standard of care. Documentation and auditing guarantee the provision of high quality care and justify the existence of the service.

2.2. *Values and preferences*

A comprehensive outreach service that includes telemedicine, mobile communication or regular satellite clinics is not always feasible, particularly in remote areas in RLS. In these circumstances, ad-hoc visits by the multidisciplinary team to these communities for direct patient care, education of the local team, and public education should be organized for these remote disadvantaged communities.

2.3. *Costs*

Although outreach services have cost implications, especially for the initial setup, they are of great value not only for patients but for both the burn centers and the communities served. For the patient, the system ensures that the right patient is treated at the right place. For the burn center, these services help to avoid unnecessary patient triage, preserving capacity for needy patients and for the community, and providing staff education and raising the standard of care. It is imperative for the burn center to show that the program achieves its objectives of providing good practice, improved outcomes, and cost-effectiveness.

Recommendation 3

Outpatient burn programs should be multidisciplinary and include wound care, scar management, functional activities and psychosocial consultation as needed.

3. Considerations in formulating Recommendation 3

Care of patients with burns that is delivered in an outpatient setting should be multidisciplinary, paying attention to the patients' physical and psychological well-being, families, and careers as well as their burn wounds. Successful wound management achieves timely healing, and avoids the risk of hospital readmission and complications such as infection or sepsis. Wound dressings that do not need frequent changes are less painful, and easy to apply and remove, thus requiring less analgesia; their use should be encouraged whenever possible, especially in the outpatient setting. Wounds should be regularly monitored until completely healed, and pain should be assessed and managed appropriately. Patients with wounds that do not heal within 2 weeks from injury should be referred to the burn center. Selection of wound dressings for superficial and partial thickness burns in outpatient settings depends primarily on the available resources and local protocols, as current evidence of clinical and cost-efficacy is poor.

Burn survivors who have left the hospital and patients with burns that were primarily treated at outpatient clinics should be closely monitored for physical and functional progress either in person or via videoconferencing with appropriately trained staff [677,678]. A rehabilitation plan (prescription) should be designed, implemented and updated according to the patients' needs. Screening of burn patients after hospital discharge for early signs of psychological distress is important in order to alleviate anxiety and other risks for these vulnerable patients [679]. This screening should be an integral part of the outpatient rehabilitation program.

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A United States national program (Burn Model System) was established in 1993 (http://burndata.washington.edu). A database of over 5000 patients was created that collected patient data from four major burn centers. The program has provided an extremely valuable resource, detailing how to identify at-risk burn survivors. To date, there are 31 publications that delineate the long-term physical and psychological impact on burns survivors. This program has created a wealth of knowledge and educational materials that are essential to rehabilitation and improving outcomes for burn survivors [680].

3.1. *Balance of benefits and harms*

Significant agreement supports the provision of multidisciplinary care after burn patients leave the hospital. Furthermore, patients who did not require hospitalization need to be reviewed in outpatient settings to screen for physical or psychological impact. Burn injury, even when minor, has a significant impact on patients and their families. A great deal of physical and psychological adjustment is needed, which requires a multidisciplinary team approach to guide patients though this turbulent time and to achieve good functional and psychological outcomes.

3.2. *Values and preferences*

Integrated multidisciplinary outpatient care within the burn service is a fundamental part of burn management and should be instated within the infrastructure of any burn care service. Not providing outpatient care would create a risk for serious negative effects on the well-being and quality of life of burn survivors. Health care providers and policymakers in some RLS may face the challenge of affording the training and resources to establish a multidisciplinary team. In these circumstances, regional training facilitated by the International Society for Burn Injury (ISBI) or other non-governmental organizations (NGOs) such as Interburns, may help to bridge this gap as long as the regional need is recognized. Modular online training is also available with minimal cost to assist in building the multidisciplinary team. Where it may not be possible to include a psychologist in the team in RLS, screening using validated tools is still appropriate, and can be performed by other team members.

3.3. *Costs*

Although the cost of providing multidisciplinary outpatient care can be challenging in RLS, the beneficial effects of this service should be balanced against the impact of lost work productivity, chronic disability, and how this will be magnified nationally in terms of gross domestic productivity.

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Electrical burns

Recommendation 1

Patients with low voltage electrical burns (less than 1000 volts) should have an electrocardiogram (ECG); otherwise, these patients should be managed similarly to any other thermal injury, adhering to admission criteria.

1. Considerations in formulating Recommendation 1

Monitoring may be necessary after electrical injury if loss of consciousness, an arrhythmia, or another documented ECG abnormality is associated with the incident.

The effect of electrical injury is related to its intensity (in amperes) which is determined by voltage and resistance. As voltage (V) is the most commonly known parameter, electrical injury is classified as either low-voltage (less than 1000 V) or high-voltage (1000 V or more) injury [681]. Low-voltage electrical injury is more prevalent than high-voltage (HV); however, there are no systematic evidence-based recommendations on these phenomena [681,682]. An ECG is recommended whenever a history includes contact with electric current, whatever its voltage [683]. If the ECG is normal, or unchanged from that before the injury, then cardiac injury is unlikely [684–691]. Whenever any abnormal finding on patient examination or the ECG is found, including any change from a previous ECG, the patient should be monitored for several hours. Monitoring may be indicated on admission, or even with a normal ECG, when the patient has loss of consciousness, cyanosis, chest pain, nausea, vomiting, and/or cardiac symptoms (palpitation, tachycardia, arrhythmia, etc.), [683–686] or when there are a pre-existing cardiac problems [692]. A carefully taken history is extremely important in cases of low-voltage (LV) injuries, because some injuries that appear to be from low voltage are actually not. Capacitors, and similar high-voltage sources in household devices, might cause HV injury [693].

Tips:

1. Cardiac marker levels—such as creatine phosphokinase (CPK), creatine kinase-muscle/brain (CPK-MB), and troponin T or I—are not sufficient alone to indicate cardiac involvement in cases of low-voltage electrical injury either in children [681,683,692] or adults [694,695]; all cardiac marker levels are likely to be disturbed by skeletal muscle destruction. Therefore, results of these tests should be interpreted with consideration to the clinical picture and risk factors mentioned above. With electric current less than 240 V, the risk of all serious complications is very rare [682,685,687,696,697].
2. Apart from cardiac arrhythmias, other injuries in the acute stage are rare in LV burns. Lung damage following exposure to 380 V electric current as well as unilateral uveitis, cataract, and retinal detachment following low-voltage (not specified) electric current have all been reported [682,698].

1.1. *Balance of benefits and harms*

Admission as an inpatient for electrical injuries must be carefully considered. Unnecessary surveillance and/or admission may be detrimental to the health care facility as well as the patient. Similarly, discharge, without confirmation of absence of risk, might lead to significant morbidity and mortality. Patients with significant symptoms benefit from monitoring, for several hours, at which time the decision to admit or discharge should be made.

1.2. *Values and preferences*

ECG is readily available in almost all emergency settings; therefore, performing an ECG for all electrically injured patients may assist in determining which patients would benefit from monitoring, and more importantly, who could be sent home safely. The extent of monitoring will be dependent on local capabilities as well as resources.

1.3. *Costs*

ECG is a valuable, nearly free, cost-effective investigation that assists in appropriate clinical decision-making; its use thus reduces the cost related to hospitalization. On the other hand, selective admission is cost-effective as it allows the best use of available resources, particularly in the overcrowded emergency department, and particularly in resource-limited settings (RLS).

1.4. *FAQs*

Q. How does one manage a pregnant woman who sustained a low-voltage electrical injury?

A: Both mother and fetus should have an initial ECG. The patient may be discharged if both ECGs are normal and both have normal examinations. As rates of complications are variable in the literature, some authors advise monitoring the fetus in all cases [681].

Q. Are patients implanted with cardiac electronic devices exposed to specific hazard(s)?

A: As in cases with external cardioversion, electrical injury might damage the integrity of the device. Therefore, these devices should be checked in all cases of electrical injury.

Recommendation 2

Patients with high-voltage electrical burns (contact with electric current more than 1000 volts) should be transferred to a burn care facility with the capability of caring for these complex patients.

2. Considerations in formulating Recommendation 2

True HV electrical burns are associated with major morbidity and mortality [693,699–701]. The high incidence of associated orthopedic, ocular, neurologic, and visceral problems dictates the necessity for a multidisciplinary approach to patient care [702]. Therefore, the burn center dealing with HV burns should have all specialties and sophisticated equipment available. Bony fractures, subluxations and dislocations may be associated with HV burns, either due to falls or convulsions [700]. Vascular injuries might be immediate or delayed (up to several weeks). Injury may be solely due to direct effect of the electricity or may result from an associated compartment

syndrome. Moreover, secondary hemorrhage might result from vascular dissection [693]. Although much less common than musculoskeletal and vascular injuries, visceral injuries, such as large- and small- intestinal injury, have been reported [703]. Because HV burns are frequently associated with significant limb injury, the complexity of HV electrical injuries necessitates burn center care [704].

Most resuscitation formula calculations are based on the burned area. As "actual" burned area is usually difficult to assess early in HV burns, these formulas might not be sufficient. Therefore, it is advised to start by using any formula and size, and then readjust according to the patient's clinical status and investigation; hence, the importance of monitoring in these cases.

In cases of HV electrical burns with suspected rhabdomyolysis, prevention, diagnosis and treatment of myoglobinuria should be implemented without delay. Myoglobinuria may cause acute kidney injury (AKI). As such, measures to ameliorate renal injury should be carried out as soon as possible. Direct injury from electric current is unusual; however AKI is one of the most commonly associated injuries in HV electrical burns [681,693,705] and it negatively influences the outcome [701,705,706]. Myoglobinuria is the presence of heme-containing protein (myoglobin) in the urine from skeletal muscle destruction (rhabdomyolysis) [707]. Recommendations for management are based on observations from retrospective studies, case reports, and case series [706]. Renal excretion of small quantities of myoglobin might pass undetected. Excretion of more than 250 pg/mL produces mahogany or dark tea-colored urine (pigmenturia), the classic clinical presentation of myoglobinuria in electrical burns. Other presentations, such as muscle pain and weakness, and hyperventilation or hypoventilation, are not reliable. In dehydrated or hypotensive patients, concentration of large quantities of myoglobin in the glomerular filtrate can precipitate tubular damage with subsequent acute renal failure.

Myoglobinuria might present with oliguria or anuria [706]. Lab diagnosis of myoglobinuria is helpful, but not definitive. Myoglobin is detected in urine only when the serum level is above 0.3 mg/L. The dipstick is positive in the absence of myoglobin and in the presence of hemoglobin (hematuria). Serum (creatine kinase) CK levels, although gradually increasing during 12 h after the onset of rhabdomyolysis, peak after at least 3 days. Serum creatinine level elevation occurs within a few days after AKI is established [706]. Therefore, clinical diagnosis is the foundation for starting treatment.

Prevention or mitigation of rhabdomyolysis in HV burns involves provision of adequate fluid resuscitation and employment of early fasciotomies when limb compartment syndromes are suspected. The goal is to limit further muscle damage and the release of myoglobin into the circulation. Appropriate early intravenous (IV) fluid therapy remains the cornerstone of rhabdomyolysis treatment and the prevention of AKI [706]. Fluids should be sufficient to maintain, in cases where a heme pigment in the urine (clear urine) is absent, an output of at least 0.5 mL/kg/h [693]. However, in cases of true HV burns with myoglobinuria, maintaining the urine output of 1.0 mL/kg/h is recommended [693,706]. If the desired rate cannot be established by fluids alone, then mannitol 25% (12.5 g/50 mL) is administered [699,706]. Use of mannitol continuous infusion, loop diuretics, and sodium bicarbonate is controversial [693,699,705,706,708]. Mannitol should be reserved for patients who do not respond to IV fluid, as it is contraindicated in anuric patients. Mannitol, in addition to causing diuresis, has other benefits, including its role as an antioxidant and vasodilator, preventing renal tubular cast deposition and expanding extracellular volume through mobilization of fluids to the circulation, thus reducing intra-compartmental pressure [706].

2.1. *Balance of benefits and harms*

The outcome of HV burns is adversely impacted by bad management, particularly by delayed referral [701]. Early transfer is vital to ensure patient safely. Whenever there is any doubt in the diagnosis of electrical injury, the patient should be considered as having HV burns until proven otherwise.

2.2. *Values and preferences*

All emergency and ambulance workers should be trained to properly diagnosis true HV burns and life/limb-threatening conditions as well as the importance of rapid safe transfer to the nearest convenient burn center. In developing countries, transportation of HV burn patients to a specialized burn center might be delayed. Therefore, all burn care facility teams should be trained to properly manage these cases. Occupational and physical therapy services should be an integral part of the center and the rehabilitation specialist should be included in the electrical burn management team.

2.3. *Costs*

High-voltage electrical injuries and burns are more prevalent in developing countries, which have fewer appropriately equipped centers [700]. As such, admission of electrical burns in RLS should be well regulated and clearly described to restrict admission to clinically appropriate cases, thus assuring a cost-effective service.

Recommendation 3

In high voltage electrical burns with myoglobinuria and/or neurologic deficits, patients should be treated in burn centers with expertise in escharotomy and fasciotomy.

3. Considerations in formulating Recommendation 5

Myoglobinuria and neurologic deficits are hallmarks of muscle damage secondary to electrical injury. Hence, it is likely that fasciotomies may be required in the involved extremities. In HV electrical injury, rhabdomyolysis develops due to a combination of direct muscle injury and compartment syndrome caused by edema within a fascial compartment; as such, electrical burns, edema, and compartment syndrome may occur in any compartments impacted by electricity [701,707]. Time between injury and manifestation varies from minutes to hours. The initial insult is a combination of direct injury from tissue damage (tissues with highest resistance are

at greatest risk) and edema leading to impaired venous return. This initiates a vicious cycle with subsequent increase in the compartmental pressure. Arterial compromise, absent distal pulses, manifests, if ever, only when the compartment pressure exceeds the systolic blood pressure, a point by which irreversible muscle damage is likely to have already occurred [708–710]. Diagnosis is based mainly on clinical picture and/or compartment pressure measurement. Peripheral nerves may be affected within 1 h [709]. Therefore, severe pain, altered sensation, pain on passive stretch, paresthesia, and paresis, are the common presentation. Nevertheless, systematic reviews have showed that these findings have low sensitivity and high specificity, giving them poor predictive value.

Although absolute compartment pressure greater than 30 mmHg is an indication for fasciotomy both in adults and children, some clinicians prefer to use the differential pressure (diastolic blood pressure minus intracompartmental pressure), with the threshold of less than 30 mmHg [709]. Muscle compartments should be opened if there is significant clinical concern, keeping in mind that muscle groups closest to the bone carry the highest risk [708,710]. Fasciotomy is the most effective intervention for decreasing pressure and improving circulation. Performing fasciotomy may prevent, or, in some early cases, mitigate muscle necrosis. Nevertheless, fasciotomy creates open wounds, with subsequent risk for infection, sepsis, amputation, and death. Routine fasciotomy is to be discouraged [711].

Tips:

Compartment syndrome should be suspected in all cases of HV electrical burns. An early sign is pain in the compartment with passive motion (passive stretching) of its muscles. Other early signs include rest pain, severe pain out of proportion to the known injury and/or not improving with adequate analgesia [702,709]. Fasciotomy should be performed within 6 h of injury if symptoms exist [706,708]. In addition to relieving pressure, fasciotomy allows exploration of the limb to assess viability; massive necrosis may mandate amputation [703,710]. Compartment pressure could be measured by arterial line transducer systems with side-port needles and slit catheters. Self-contained measuring systems are the most accurate [709].

3.1. *Balance of benefits and harms*

Inadequate decompression negatively impacts HV burn outcome [701,710,711]. Furthermore, missed compartment syndrome might lead to additional legal consequences [709]. These create a difficult dilemma for the clinician, especially in cases where symptoms are not clearly diagnostic. Clinicians should maintain a high index of suspicion for muscle injury and should respond accordingly. A missed injury may result in loss of life or limb. However, fasciotomy is not without risks, including nerve and muscle injury and subsequent scarring. Only providers trained in the performance of fasciotomy should perform this procedure in HV-injured patients.

3.2. *Values and preferences*

Different practitioners have different levels of expertise, which may limit the performance of invasive procedures. Fasciotomy is indicated whenever gross myoglobinuria and metabolic acidosis persist and muscle necrosis is suspected [706,711]. Muscle necrosis may be evident at the time of surgical release, and this will necessitate serial re-looks and debridements and even amputations following completion of the acute resuscitation [709].

3.3. *Costs*

Laboratory diagnostic tests in HV electrical burns, such as CPK and troponin testing, are not reliable indicators on the extent of injury. Therefore they are not cost-effective. Moreover, myoglobinuria, but not other data, usually can be assessed immediately upon admission [702]. Similarly, compartment pressure measures, although highly specific, might be deceiving, and do not exclude the presence of muscle necrosis. The value of these measures is that they are of low cost, may be repeated, and are available in virtually every setting.

Recommendation 4

Extensive rehabilitation may be required for optimal recovery after electrical injury.

4. Considerations in formulating Recommendation 4

Morbidity after electrical injury is high and physical and psychological sequelae are common [712]. Electrical injury, particularly HV injury, frequently results in severe damage to not only the skin, but also the muscles, bones and nerves. Amputation of limbs, damage to the peripheral and central nervous system, and concomitant trauma (bone fractures, etc.) associated with electrical injury result in more complex rehabilitation needs for the patient [713–716]. Such physical injuries, in conjunction with neuropsychological changes, result in impairment and functional limitation, and disability and rehabilitation services are necessary for optimal recovery [717].

An electrical burn injury may affect multiple body systems including neurologic, musculoskeletal, respiratory, cardiovascular, and urinary systems; a comprehensive and coordinated team approach to the short- and long-term management of patients is necessary [716]. Concomitant traumatic injuries may result directly from the electric current (for example, burst fractures) or from subsequent falls (e.g., spinal cord injury) during the electrical incident. Patients with electrical injury should be carefully screened for such injuries before beginning a rehabilitation program. Neurologic injuries from electrical burn may be temporary or permanent and may have immediate onset at injury or delayed onset up to 2 years after injury [714,718]. A thorough neurologic examination is necessary and ongoing monitoring of neurologic function is recommended. However, in LV injury, diagnostic testing is not always conclusive and may not correlate with neurophysiologic symptoms [719].

If impairment or functional limitations occur due to electrical injury or its sequelae, early rehabilitation should be initiated to prevent further problems and accelerate return of function [716]. Patients who require amputation after electrical injury should receive early rehabilitation services including pain

management, prevention of deformity, strengthening, functional retraining, and psychosocial coping [720]. The goal of rehabilitation after an electrical injury is to help the patient return to the highest level of function possible. Adaptive equipment may be used or methods taught to patients to help them achieve functional goals and assist them in returning to their premorbid level of functioning when possible [721,722]. In the case of permanent loss of muscle mass, function and/or strength, rehabilitation should include strengthening of other muscle groups and retraining of functional skills with adaptations for maximal independence. Burn survivors with electrical injury should be evaluated for changes in cardiopulmonary function and monitored carefully with exercise and increased activity during rehabilitation.

Neurocognitive changes have been associated with electrical burn injury [723,724]. Disability after electrical injury may be related to a patient's loss of physical abilities or due to the occurrence of psychological or psychiatric sequelae. A comprehensive rehabilitation program for a burn survivor after electrical injury includes psychological and psychiatric evaluation and treatment. Occupational groups are at highest risk for electrical burns [725]. Rehabilitation services specializing in electrical injury can help a burn survivor return to the work force [715]. Social support to the patient by family and friends should be facilitated after electrical burn injury for improved community reintegration [726].

4.1. *Balance of benefits and harms*

Addressing the complex rehabilitative needs of a patient who has sustained extensive electrical burn injury involving multiple tissues and organs may require more time and resources than a patient with a typical thermal-only injury. Rehabilitation should focus on remedying functional problems as a result of sequelae from the burn injury (e.g., amputation, neuropathy, fracture, muscle function loss). The benefit of providing rehabilitation services after electrical injury is that it provides the burn survivor with the opportunity to recover function or learn modified function that can help them gain independence and have greater capacity to return to their life roles.

4.2. *Values and preferences*

Although HV burns are devastating, early physical and occupational therapy significantly reduces limb dysfunction [727]. Furthermore, social, psychological, occupational and functional rehabilitation are similarly effective to return the patient to the community with the least possible sequelae.

4.3. *Costs*

Because young men, who are at their prime earning potential, are typically at highest risk for electrical injuries, and in particular HV injuries, this has a significant social and economic impact [728,729]. Providing rehabilitation services can help patients recover more fully from their injuries and offers greater potential for return to work and life roles. Many countries have advocated for prevention and educational campaigns, particularly with occupational groups, to promote safety and electrical burn prevention in the hope of reducing the economic impact of electrical burns. Prosthesis and orthosis required as part of a rehabilitation regimen can be expensive and complex, but low-cost, creative alternatives are available and can improve a patient's function using locally available resources to fabricate adaptive devices [722].

4.4. *FAQs*

Q. If an electrical injury has resulted in amputation and skin grafting on the residual limb, will the burn survivor be able to wear a prosthesis?

A. Although the time until prosthetic fitting may be delayed, burn survivors with amputation and skin grafts on their residual limbs have been shown to be able to wear lower- and upper-extremity prostheses and recover the ability to walk and perform activities of daily living [730].

Q. Does the head need to come in contact with the electrical source for there to be neurocognitive changes?

A. No. Cognitive changes including decreased attention, poor memory, reduced executive brain function and personality changes have been shown to be associated with electrical injury incurred at places besides the head.

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Chemical burns

Recommendation 1

Removal of the chemical agent should be done immediately to mitigate ongoing injury to skin and absorption of the chemical.

1. Considerations in formulating Recommendation 1

Throughout the developed and developing world, intentional and unintentional chemical injuries to skin, lungs, and eyes, and systemic toxicity, are a frequent occurrence. In one recent review, roughly 10% of cutaneous burns and 30% of burn fatalities at a major burns unit were found to be related to chemical injuries [731].

The severity of a chemical injury is related to duration of skin contact and agent concentration. Hence, in any setting, the primary intervention is to limit the exposure to the offending agent. This common-sense expediency remains unchanged over decades of peer-reviewed commentary on management of chemical injuries [732]. Chemical burns should not be neutralized, as this can result in generation of heat and extension of injury. Powders should be brushed away, and liquids should be rinsed off after clothing is removed.

1.1. *Balance of benefits and harms*

The urgent removal of a noxious chemical agent from both the patient and the patient's environment is not just beneficial but compulsory if effective rescue of those injured is to be realized. However, there are tangible and outsized risks to both victims of chemical exposure and to their health care providers [733]. Decontamination before permitting entry into the hospital is important, and if done poorly, can result not only in rescuer injury, but also can effectively shut down any ability to further care for the injured. To be sure, there are fixed and substantial costs associated with having the necessary kit and space for a fully-fledged capability to decontaminate prior to admission to care areas [734].
Appropriate protection for those responsible for decontamination must be carefully considered and is a bedrock principle in the medical management of all nuclear, biologic, and chemical events [735].

1.2. *Values and preferences*

Irrespective of local customs and general resource levels, common-sense measures to stop further exposure to the offending noxious chemical are available and adaptable to any and all local circumstances.
The availability of a chemical burn kit and policies regarding its use are likely to vary widely based on financial resources and local chemical-injury patterns. Providing care adjacent to heavy industrial settings is an example of such local specific preplanning.
Some societies currently see more chemical injuries than the global average; such injury patterns have appropriately called attention to themselves from a public health perspective [736].

1.3. *Costs*

The actual global financial burden resulting from chemical burn morbidity and mortality is unknown. However, based on the relative fraction of all injuries managed in burn centers, this burden is unquestionably sizeable [731]. Compulsory decontamination facilities and protocols represent a cost component that must be absorbed.
Some efforts exist to link occupational injuries to chemical concerns, and this approach may be an underutilized legitimate means to underwrite the expense of care [737].

Recommendation 2
After removal of the inciting agent, burn wound care should follow. Initial care should include irrigation with cool running water to remove residual chemicals prior to application of dressings.

2. Considerations in formulating Recommendation 2

Although aqueous dilution is not a panacea for all noxious chemical agents, a significant majority of agents are water soluble, and for many, copious aqueous dilution is the most effective primary mitigation [738]. Flush the area with clean running water for at least 20 min, and if there is still a burning sensation, flush additionally for another 10–15 min. Hypothermia can be a risk if excessively cold water is used.
One important consideration is the ability to adequately care for a mass casualty influx of chemical exposure victims including the logistics of providing safe aqueous irrigation for a large number of cases while not creating the risk for hypothermia, ensuring a clean source of water, and providing adequate patient privacy [739,740].

2.1. *Balance of benefits and harms*

For many chemical agents, aqueous dilution is the significant portion of the required initial treatment. For those agents that are not water soluble, aqueous irrigation still removes bulk material. Potential harms include hypothermia and possible contamination with waterborne microbes, but applied common sense can prevent these problems [739,740].

2.2. *Values and preferences*

There are parts of the globe where water, especially in the volumes required for chemical dilution, are simply not available—for instance in desert climates. Elsewhere, the problem may not be lack of water, but lack of water free from microbial pathogens. With chemical wounds, the natural intact skin barrier to microbes is breached, and in certain circumstances the risk of nosocomial infection outweighs the benefits of aqueous irrigation.

2.3. *Costs*

Although clean water may be a luxury in some settings, it is something that hopefully would be readily available in any health care setting if its need is reasonably anticipated as part of best practices [741]. Costs of large volumes of clean water may vary from essentially free to essentially unobtainable.

Recommendation 3
Chemical agents have unique systemic and pulmonary effects which may have delayed onset. These effects must be considered in the management of the patient exposed to chemical burns.

3. Considerations in formulating Recommendation 3

Many encountered noxious chemical agents have a very high vapor pressure, or exist at terrestrial barometric pressures and temperatures as gasses; they therefore represent inhalation injury agents as well [742–744]. Specifically, concentrated inorganic acids, phenol, phosgene, vesicant chemical warfare

agents, chlorine, anhydrous ammonia, and hydrogen sulfide can all cause pulmonary injury from inhalation.
Additionally, many chemical agents are inherently toxic to cells and organs via systemic means, and some are readily absorbed through the skin and into the bloodstream [745–747]. These include phenol, phosgene, vesicant chemical warfare agents, white phosphorus, hydrofluoric acid, and hydrogen sulfide.

3.1. *Balance of benefits and harms*

Recommendation 3 is formulated to underscore the potential systemic and pulmonary damage from chemical agents—the clinician needs to anticipate toxicities remote from the skin itself, and not fall prey to an excessively narrow clinical focus when dealing with these agents. A delay in diagnosis of systemic and pulmonary sequelae can lead to irreparable harm.

3.2. *Values and preferences*

Patterns of chemical injuries definitely vary around the globe. Some countries are very industrialized [748]. Others unfortunately are suffering under the criminal use of chemical warfare agents [749]. Some patterns of systemic and pulmonary injuries from chemical agents in these local settings that can be recognized and anticipated such that a more positive impact on morbidity and mortality can be achieved.

3.3. *Costs*

The actual cost of chemical burn injuries is unknown, although attempts to characterize the financial burden have been made [737]. Other studies on the economics of the methamphetamine crisis and chemical ocular injuries, while not precisely concerning systemic and pulmonary toxicity of chemical injuries, do provide a tangential estimate of the cost burden

Table 4 – Common chemical agents, their characteristics and treatment.

Chemical agent	Description/injury pattern	Treatment
Cement [752,753]	Strong alkali with pH 12-14	Perform copious water irrigation
Muriatic (hydrochloric) acid and sulfuric acid [754]	Strong inorganic acids	Perform copious water irrigation; do not neutralize with base
White phosphorus [755]	Military munition; spontaneously ignites upon exposure to air; generates corrosive phosphoric acid	Keep wound soaked with water until particles can be removed; perform copious water irrigation; remove embedded particles (may require surgical excision); use Wood's lamp to facilitate particle identification; monitor for hypocalcemia and treat if present.
Strong alkali (NaOH, KOH) [756]	Denatures biomolecules into water-soluble forms that then perpetuates deeper involvement of tissues below (liquefactive necrosis)	Perform copious water irrigation
Phenol (carbolic acid) [757]	Readily absorbed through skin and across lungs; causes central nervous system toxicity and cardiac dysfunction	Remove from skin with polyethylene glycol (PEG), isopropanol, or glycerol
Mustard agent [742,746]	Chemical weapon; blistering agent and inhalation hazard. Vapor or oily liquid; heavier than air; lingers in environment persistently. May cause aplastic anemia and/or pancytopenia.	Decontaminate and remove with copious water irrigation, care of blistered skin wounds
Chlorine [743]	Common industrial chemical; gas. Causes irritant-induced asthma and reactive airways dysfunction syndrome (RADS). High concentrations can cause acute respiratory distress syndrome (ARDS) or injure skin.	Decontamination and removal with copious water irrigation; supportive pulmonary care
Anhydrous ammonia [758]	Common industrial reagent, transported in a liquid state −33 °C (−28 °F); strong alkali (see above); inhalation injury hazard; may cause frostbite injury.	Perform copious water irrigation; treatment of frostbite and strong alkali injury; supportive pulmonary care
Phosgene ($COCl_2$) [759]	Chemical weapon and common industrial reagent. Poisonous gas that stays low to the ground. Causes pulmonary edema which may present up to 48 h after exposure.	Move to high ground, decontaminate with soap and water; monitor closely; supportive pulmonary care
Hydrogen sulfide [760]	Produced by decaying organic matter (e.g., manure); seen in oil and gas industry. Mucous and respiratory tract irritant; may cause CNS toxicity with rapid unconsciousness and death; low-grade skin irritant	Supportive care; consider hydroxocobalamin (Cyanokit®)
Hydrofluoric acid [761]	Unique inorganic acid widely used in industrial applications including rust removal and glass etching; if absorbed systemically, may cause life-threatening hypocalcemia.	Perform copious water irrigation and topical application of calcium-containing gels. Severe cases may need calcium injection into tissues, or delivery intra-arterially or via venous Bier block. Monitor for hypocalcemia and treat if present

suffered [750,751]. Treatment costs spike dramatically if victims require hospitalization, acute surgical management for reconstruction, and/or ventilatory support (in instances of pulmonary toxicity or respiratory failure from systemic illness).

Recommendation 4
Apply countermeasures for specific agents, as shown below.

4. Considerations in formulating Recommendation 4

Following are several common chemical agents that have specific injury patterns and unique best-practice antidotes (Table 4).

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